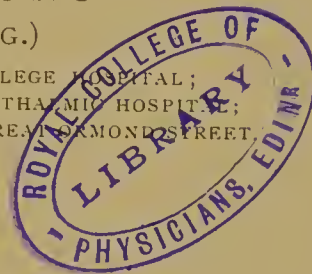U. 5. 34.

THE PATHOLOGY OF THE EYE

THE

PATHOLOGY OF THE EYE

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VOLUME III

GENERAL PATHOLOGY.—PART I

HODDER AND STOUGHTON

PREFACE TO VOLUME III

THIS volume commences the discussion of the General Pathology of the Eye. It includes Congenital Abnormalities, Ametropia, the Circulation and Nutrition of the Eye, the Normal Intra-ocular Pressure, and Glaucoma. Bearing in mind the fact that pathology is but physiology modified by abnormal conditions, I have considered it essential to give an exhaustive account of the normal circulation and nutrition of the eye. It is scarcely necessary for me to express my indebtedness to the writings of Professor Leber upon this subject, more especially to his *résumé* in the second edition of the 'Handbook' of Graefe-Saemisch. Since 1865, when he published his description of the anatomy of the intra-ocular blood-vessels, Professor Leber has been a pioneer in this field of discovery. The problems which he has solved by his exact researches are of fundamental importance, and those which yet await solution must be attacked with the weapons which he has provided.

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ABBREVIATIONS

A. d'O.—Archives d'Ophthalmologie.

A. f. A.—Knapp and Schweigger's Archiv für Augenheilkunde. (Articles in A. f. A. are often translated or abstracted in A. of O., and *vice versâ*; the reference is usually given to one only.)

A. f. O.—v. Graefe's Archiv für Ophthalmologie.

A. of O.—Knapp's Archives of Ophthalmology.

B. d. o. G.—Bericht der ophthalmologische Gesellschaft zu Heidelberg. (The earlier reports are contained in K. M. f. A.)

B. z. A.—Deutschmann's Beiträge zur Augenheilkunde. (The reference is given to the part [Heft], not to the volume.)

C. f. A.—Hirschberg's Centralblatt für praktische Augenheilkunde.

G.-S.—Graefe-Saemisch, Handbuch der gesamten Augenheilkunde. (The date determines the edition: 1st edition, 1874—1877; 2nd edition, 1898—   .)

K. M. f. A.—Zehender's Klinische Monatsblätter für Augenheilkunde.

R. L. O. H. Rep.—Royal London Ophthalmic Hospital Reports.

T. Am. O. S.—Transactions of the American Ophthalmological Society.

T. O. S.—Transactions of the Ophthalmological Society of the United Kingdom.

Z. f. A.—Zeitschrift für Augenheilkunde.

*.—The most important articles are marked with an asterisk (*).

CHAPTER XIV

CONGENITAL ABNORMALITIES

UNDER the designation "congenital malformations" may be included all those abnormalities which are present at birth and are due to arrested or aberrant development. In accordance with the general scheme of this work conditions affecting individual parts of the eye will be first considered, then those affecting several structures, *e. g.* colobomata, and finally those affecting the eye as a whole.

Ætiology.—Very little is known as to the causation of congenital defects. The defects themselves are characterised by two chief features—delay or arrest of normal development, and aberrant development. Of these, the former is by far the more prominent, and since ontogeny is a compressed phylogeny some cases may be regarded as atavistic, or reversions to lower types. Any condition which impedes growth might be expected to act deleteriously upon the delicate foetal structures. Injuries, pressure, changes in temperature, changes in the chemical constitution of the circulating fluids, etc., all probably play their part. Hertwig's experiments are interesting in this connection : he found that 0·6 per cent. salt solution delayed the development of the medullary ridges in frog embryos, and that 0·6—0·8 per cent. salt solution delayed the closure of the medullary canal in axolotl embryos. Brown-Séquard observed corneal and lenticular opacities in the offspring of guinea-pigs in which the restiform body had been divided ; these results are probably fortuitous.

In most cases the abnormalities can be explained upon one of two grounds—simple arrest of development, or intra-uterine inflammation. Many cases which are almost or quite impossible to explain on the first theory are readily explained by the second. There can be no doubt, however, that the logical position to adopt is that of calling in the aid of inflammatory processes only when the conditions are such that simple arrest of development fails to account for them. The view of Deutschmann, that all congenital abnormalities are due to inflammatory processes, goes much too far, whilst the opposite opinion, that none are due to these processes, involves a straining of facts which is unreasonable.

Both theories offer very great difficulties. There is no satisfactory explanation of the cause of arrested development ; the suggestions

already made are reasonable, but almost entirely conjectural. That arrest of development occurs in the absence of any inflammatory phenomena cannot be doubted, and is supported by the analogy of congenital malformations in other parts of the body. Heredity is found to be comparatively rare. It is commonest in irideremia, and has been found in a few cases of microphthalmia; it is quite rare in colobomata (E. v. Hippel). A priori it may be stated that the abnormalities must be due either to inherent defect in the germ or to deleterious external agents acting upon a normal germ. The former condition cannot at present be explained. Defective development of blood-vessels may have a widespread effect (Treacher Collins). There are certain deleterious conditions, other than actual fœtal inflammation, which merit mention. Such are diseased conditions of the placenta or uterine mucous membrane, and diseases transmitted from the mother to the child by way of the blood-stream. These errors of nutrition are brought about by chemical agents, and are for the most part essentially inflammatory in their ultimate origin.

The ocular abnormalities have been considered to be secondary to defective development of the brain. Microphthalmia, for example, is generally associated with microcephaly. It is more probable that both are due to the same cause (e. g. Rindfleisch, Bernheimer). There are cases, too, of embryos with extensive defects of the brain in which the eyes have been well developed.

Abnormal conditions of the amnion probably account for some malformations, though van Duyse goes too far in attributing polycoria, aniridia, atypical iris colobomata, corectopia, and luxation of the lens to pathological conditions in the amnion (cf. Vol. I, p. 135).

The question of intra-uterine inflammation is surrounded with difficulty. In the first place, as Marchand has pointed out, the term "inflammation" must be used in a wider sense than usual, for there can be no question of inflammation in the restricted sense in early embryonic life, because that involves conditions of the tissues, e. g. a fully developed vascular system, which are as yet absent from the embryonic structures. Probably the most conclusive evidence in favour of intra-uterine inflammation as a cause of congenital malformation is to be found in congenital anterior staphyloma.

All these cases of congenital anterior staphyloma show exactly the same features as are found when the condition develops in the usual manner after birth. A priori, therefore, we should be naturally inclined to attribute them to the same cause. More minute investigation will confirm this view, though it must be admitted that there are special difficulties which have to be faced and explained.

The ordinary anterior staphyloma results from perforation of the cornea, following ulceration. If therefore we adhere to the view expressed, we must admit the possibility of intra-uterine perforation of the cornea. This offers considerable difficulty. Traumatic perforation, if not absolutely beyond the bounds of possibility, is very improbable. Can intra-uterine ulceration of the cornea occur? We are forced to the conclusion that it can and does. Not only are these cases most reasonably explained in this manner, but there are others, such as con-

genital opacities and adherent leucomata, which cannot well be accounted for on any other hypothesis.

The chief difficulties in the way of accepting intra-uterine corneal ulceration are as follows. The cornea is a structure which the researches of Leber and Schöbl have shown to remain unvascularised throughout fœtal life, with the exception of the peripheral capillary loops. Endogenous infection through the blood-stream is therefore put out of the question—at any rate, as far as actual bacterial invasion is concerned. It is true that toxins may still escape, enter the lymph-stream, and so reach the non-vascular parts of the cornea. Here the very absence of blood-vessels may cause diminished capacity for resistance, and it is conceivable that necrosis may thus arise.

If this method be considered too improbable, infection can only occur by exogenous means—i. e. through the amniotic fluid which surrounds the fœtus. This is on the whole the more probable view, and it is supported by the comparative frequency of the cases in which bilateral ocular disease is reported. It is not surprising that both corneæ should be attacked, and if one eye succumbs more readily than the other, the condition of staphyloma may be expected to pass on into one of panophthalmitis, and ultimately phthisis bulbi, which in these cases is commonly described as microphthalmia.

There can be no doubt that intra-uterine transmission of infection from mother to child can take place. It is known that anthrax, glanders, tubercle, typhus, pneumococcus, streptococcus, and *Staphy-lococcus aureus* can be transmitted to the fœtus. It is further known that intra-uterine panophthalmitis can occur. The most important case has been published by Leber and Addario, in which congenital panophthalmitis in a goat was proved to be due to a bacillus having the morphological characteristics of the *B. diphtheriæ* (Vol. I, p. 53). Most cases of microphthalmia are attributed on the Continent to intra-uterine phthisis bulbi, and Panas considered that one such case was due to variola in the mother.

Several cases of gonorrhœal ophthalmia, occurring at birth, have been recorded. In Parischeff's case the membranes ruptured three days before birth; in Nieden's the fœtus was expelled in the intact membranes (Vol. I, p. 42). It must be admitted that these cases are not wholly free from the possibility of *post-partum* infection, though there is much to be said against that view.

Is it possible that in these cases of anterior staphyloma the infection could have occurred at birth, or *per vaginam* during parturition? The cases of Hirschberg and Birnbacher and of Runte, in which the children were seen half an hour and half a day respectively after perfectly natural confinements, prove that this cannot have happened. It is extremely improbable in the case which I have recorded (*v. infra*). Even had infection occurred then, it is inconceivable that an anterior staphyloma could have developed in the time. Fuchs has recorded the case of a child born with blennorrhœa and a perforated cornea. This might, indeed, be ascribed with some show of reason to *intra-partum* infection, but not the staphylomatous cases.

If intra-uterine infection and inflammation are eliminated, we are

thrown back upon mal-development. It is difficult to imagine how this can be brought to explain the phenomenon. Deficient development of the centre of Descemet's membrane might lead to imbibition of fluid by the *substantia propria*, and weakening of the cornea, followed by ectasia. This does not seem a likely occurrence. The endothelium, and Descemet's membrane, which is derived from it, are morphologically part of the uveal tract. In these cases there is not the slightest evidence of arrested development in any other part of that tract. The ciliary body and choroid are normally developed, and there is no reason to suppose that there has been any failure on the part of the iris—it has merely undergone the degenerative changes which we expect to find in an anterior staphyloma. Moreover, Descemet's membrane itself has developed quite normally at the periphery, and has attained the thickness which we should expect to see. Even with any such hypothesis, it would still be simpler to have recourse to inflammatory changes, producing degeneration in the endothelium, and resulting in a so-called "internal ulcer," which has been held by E. v. Hippel to account for other congenital malformations. In any case, even if the primary cause be mal-development, it is necessary to explain the very marked inflammatory changes which were undoubtedly present in my case and in some of the others. This must be intra-uterine—or, if *intra-partum*, it must submit to the criticism which that explanation involves. Again, mal-development alone will not account for the vascularisation of the cornea which is found in some of the cases, nor for the absence of epithelium over the surface of the pseudo-cornea.

If one congenital anomaly of the eye can be definitely proved to be due to intra-uterine inflammation, then that factor must receive full consideration in dealing with other congenital anomalies.

It is probable that a considerable number of conditions are described as congenital which are not so strictly. Injuries to the eye received at the time of birth account for some of these conditions, possibly, for example, for some corneal opacities and for some retino-choroidal conditions (atypical colobomata).

HERTWIG.—Arch. f. mikr. Anat., xliv, 1895. BROWN-SÉQUARD.—Comptes rendus de l'Acad. des Sciences, xciv, 1882. DARESTE.—Production artificielle des Monstruosités, Paris, 1891. DEUTSCHMANN.—K. M. f. A., xviii, 1880; xix, 1881. *E. v. HIPPEL.—In G.-S., 1900. RINDFLEISCH.—A. f. O., xxxvii, 3, 1891. BERNHEIMER.—A. f. A., xxviii, 1894. VAN DUYSE.—A. d'O., xv, 1895, MARCHAND.—Eulenburg's Real-Encyclopädie, Art. "Missbildungen," 1897. LEBER.—Untersuch. über die Blutgefässe des mensch. Auges, Wien, 1868. LAWSON.—Med. Times and Gaz., 1875. THIER.—B. d. o. G., 1896. SCHÖBL. —C. f. A., x, 1886. LEBER AND ADDARIO.—A. f. O., xlviii, 1, 1899. FÉRÉ.—Comptes rendus, 1894. PARISCHEFF.—In Nagel's Jahresbericht, 1892. NIEDEN.—K. M. f. A., xix, 1891. PARSONS.—T. O. S., xxiv, 1904. *VAN DUYSE.—A. d'O., xxiv, 1904; Encyclopédie franç. d'O., ii, Paris, 1905.

THE LIDS.

Coloboma of the lids.—Colobomata of the lids are usually triangular defects, the apex being directed towards the orbital margin: they are occasionally quadrilateral (Goldzieher). The transition to the normal lid margin is generally rounded, rarely sharp. Usually the

whole thickness of the lid is involved, but the abnormality may be continued towards the orbital margin as a cicatricial band; the tarsus may be defective where the skin and conjunctiva are still present. The edges are covered with soft, reddish conjunctiva, which unites the lid loosely to the bulbar conjunctiva. The eyelashes stop at the angles, and often markedly converge here. When they continue across the gap (*e. g.* v. Ammon, Gallenga) it is probably not a true coloboma but a

FIG. 548.—COLOBOMA OF LIDS, ETC.

Harman, T. O. S., xxiv. Right side: Coloboma of upper lid, dermoid down and out, dermo-lipoma down and out, one supernumerary ear, macroglossia. Left side: Coloboma of upper lid, coloboma of iris and choroid down and in, three supernumerary ears. Large fovea sacralis.

mere distortion. The Meibomian glands are also absent in the coloboma.

About 100 cases have been described. The first was observed by Banister (18th century) and reported by Wilde. Dor and Nicolin collected 46 cases; 27 had one lid affected, 16 one lid of each eye, 2 both lids of one eye, and 1 all four lids. The gap is usually situated to the inner side of the middle line, and it is usually a portion of the inner

part of the upper lid which is absent. The defect may be a small indentation of the free border, or may extend from the palpebral to the orbital margin. Two or more defects may occur in the same lid. There is often a defect in the orbital margin at the site of the coloboma, and coloboma of the upper lid may extend into the eyebrow, the hairs being absent or scanty. In some cases the hairy scalp projects downwards as a triangular bridge towards the coloboma (Schleich, Nuel).

In a considerable number of cases the coloboma is filled with a bridge of skin which links the lid to the globe (Manz, Nuel, Zeilendorf), and may extend on to the cornea as a form of conjunctival dermoid (q. v.). The bridge consists of true skin, containing papillæ, fat, hairs, sebaceous glands. Hairs and sweat-glands were absent in the case described by Nuel. The movements of the globe may be much impeded by the bridge.

Even in the absence of a bridge of skin there is often a dermoid or dermo-lipoma in the globe (27 times in 65 cases, Fricke) in the situation corresponding with the coloboma. There may be several dermoids on the globe (Talko, Schiess-Gemuseus). More rarely structures resembling pterygia are seen (Wilkinson, Zeilendorf), especially in the very rare cases in which the outer commissure is absent.

Colobomata of the lids are generally associated with other congenital defects of the eyes and of other parts of the body. Such are opacities of the cornea (Gallenga, Fricke), keratoconus (Creutz), corectopia (Talko), coloboma of the iris (Heyfelder, Schiess-Gemuseus), persistent pupillary membrane (in one case adherent to the back of the cornea, van Duyse). The lacrymal passages are generally normal, though in coloboma of the lower lid two puncta, medial and temporal to the coloboma, have been observed. The lids may show other abnormalities—dermoid (Talko), amniotic bands (v. Bruns, Lannelongue), oculo-palpebral synechiæ (Morian, Panas), symblepharon (Brinckmann), blepharoptosis (Cunier), coloboma of the eyebrow (Schleich, Nuel, Fricke, Gallenga, Zeilendorf).

Cutaneous growths may be present in the coloboma and neighbouring parts of the lid, and accessory auricles on the side of the face are common. Very important are the cases associated with oblique fissure in the face (e. g. Kraske, Morian, Panas, Broca, van Duyse). Here the coloboma is usually the prolongation of the fissure. Two kinds of fissure are found. The typical one is due to imperfect closure of the cleft between the frontal (mesial and lateral nasal) and maxillary processes. Atypical fissures are found in positions in which there is no fœtal cleft ; they are probably due to the pressure of amniotic bands, and this may account for the failure of the normal clefts to close. Owing to the oblique direction of the fissures the coloboma in the upper lid is usually more temporal than that in the lower lid. The fissure may be represented only by a fibrous scar to which the coloboma forms the termination.

There is a small group of cases in which the notch is in the outer part of the lower lid (Berry, Treacher Collins). It is then often

associated with mal-development of the malar bone, and is frequently bilateral.

Many of the abnormalities in other parts of the body are accounted for by the pressure of amniotic bands, such as spontaneous amputation of the extremities, syndactylism, etc. Hare-lip, cleft palate, macrostoma, exencephaly, hemicephaly, anencephaly, ventral hernia, etc., are also met with.

Various theories have been adduced to account for colobomata of the lids. They cannot be due to arrested development (Heyfelder),

FIG. 549.—COLOBOMA OF LIDS.
Treacher Collins, T. O. S., xx. Symmetrical notches in outer part of each lower lid, with defective development of malar bones.

since the lids do not develop from two lateral segments. Ewetzky, however, supports this theory on the grounds that the epithelial union of the lid margins commences at the commissures and gradually extends towards the middle. Manz held that " heterotopic tissue-metamorphosis," leading to the formation of a cutaneous bridge, impeded the proper advance of the duplicature of skin, which, springing from the orbital margin, forms the lid. These explanations can only apply to individual cases.

E. v. Hippel points out that the defect may be due either to some

cause preventing development or to some cause destroying part of the well-developed lid. The common cause for both results has been found by van Duyse in the pressure of amniotic bands, and this theory seems the best suited to explain the greatest number of facts. Not only does it explain the colobomata, but it also explains the cutaneous bridges, dermoids, etc.; these are persistent portions of the constricting bands. The objection that amniotic bands do not account for symmetrical colobomata is met by the observations of v. Bruns, Pollailon, and Lannelongue, who observed such bands inserted into the middle of the cornea and passing symmetrically over the lids.

Mayor.—Thèse de Montpellier, 1808. Heyfelder.—v. Ammon's Zeitschrift, i, 1831. v. Bruns.—Handbuch d. prakt. Chirurgie, Tübingen, 1859. Wilde.—Dublin Quarterly Jl., 1862; An Essay on Malformations, etc., London, 1862. Wilkinson.—Path. Soc. Trans., 1872. Streatfield.—R. L. O. H. Rep., vii, 1873. Pollailon.—Gaz. des Hôp., 1874. Kraske.—Arch. f. klin. Chir., 1876. Ewetzky.—A. f. A., viii, 1879. Schleich.— Mittheil. aus d. ophth. Klinik, Tübingen, 1880. Nuel.—A. d'O., i, 1881. van Duyse.— Ann. d'Oc., lxxxviii, 1882. Lannelongue.—Arch. gén. de Méd., 1883. Lang.—T. O. S., vi, 1886. Morian.—Arch. f. klin. Chir., xxxvii, 1887. Nicolin.—Thèse de Lyon, 1888; Ann. d'Oc. (van Duyse), c, 1888. Dor.—Rev. gén. d'O., 1888; Trans. Internat. Congress, Heidelberg, 1888. Panas, Broca.—A. d'O., ix, 1889. Berry.—R. L. O. H. Rep., xii, 1889. Fricke.—Berliner klin. Woch., 1889. Cowell.—T. O. S., xi, 1891. Juler.—T. O. S., xii, 1892. Hoppe.—A. f. O., xxxix, 3, 1893. *Zeilendorf.—Wiener klin. Woch., 1894. Goldzieher.—C. f. A., xix, 1895. van Duyse and Rutten.—A. d'O., xvii, 1897. E. v. Hippel.—In G.-S., 1900. Treacher Collins.—T. O. S., xx, 1900; xxii, 1902; xxv, 1905. Lang, Frost.—T. O. S., xxi, 1901. Tyrrell, Doyne.—T. O. S., xxiii, 1903. Harman.— T. O. S., xxiv, 1904. *van Duyse.—Encyclodédie franç. d'O., ii, Paris, 1905 (Bibliography).

Symblepharon.—Apart from the cases of cryptophthalmia and the partial symblepharon which is found sometimes associated with coloboma of the lid, adhesion of the lid to the globe is almost unknown as a congenital anomaly.

Ankyloblepharon.—Union of the edges of the lids is found in cryptophthalmia and in many cases of anophthalmia. *Blepharophimosis*, or partial ankyloblepharon affecting the outer angle, is not very uncommon, and is usually associated with small or deep-set eyes.

A priori it would not seem surprising if ankyloblepharon were a common malformation, seeing that the lids are so long united during intra-uterine life and separate so late. It must be remembered, however, that the union is purely epithelial.

As to the cause of ankyloblepharon it is possible that the size of the eye and the configuration of the orbit may be of importance. The pressure of the globe may be necessary to induce the normal separation, and in the absence of that pressure abnormal processes—inflammatory or other—may lead to firm fusion.

Ankyloblepharon filiforme adnatum has been observed in four cases, one of which was bilateral (v. Hasner, Bunzel, Wintersteiner, Webster). In this condition the lid margins are united by a moderately extensile band, consisting of vascular fibrous tissue covered with epithelium. The band expands somewhat at its attachments to the lids. That it is not a simple defect in separation of the lids is shown by the vascular mesoblastic tissue within it. It has been attributed to injury—*e. g.* with the finger-nail. v. Hasner attributed it to a patho-

logical growth of the skin, as similar growths were present on the cheek in his case.

TRAVERS.—Synopsis of the Diseases of the Eye, 1820. MIDDLEMORE.—Treatise, ii, 1835. V. HASNER.—Prager Zeitschr. f. Heilkunde, 1882. BUNZEL.—Prager med. Woch., 1890. DE HAAS.—Med. Weekblad., 1894. WINTERSTEINER.—C. f. A., xxii, 1898. WEBSTER. —B. z. A., xxxiv, 1898.

Cryptophthalmia.—This very rare condition consists of total congenital ankylo- and sym-blepharon, but there is also invariably abnormality of the eyeball and often of the orbit, etc. The first case of cryptophthalmia was recorded by Zehender and examined anatomically by Manz (1872). Cases have since been recorded by Hocquart, Chiari, van Duyse (2), Fuchs, Otto, Bach, and Karmann : seven have been examined anatomically.

In cryptophthalmia the skin passes continuously from the brow over the eye to the cheek. Some indication of the palpebral fissure is almost always present as a shallow linear depression or as a white line of scartissue. The eyelashes are always absent. There is sometimes a small depression in the situation of the palpebral aperture : in Hocquart's case folds of skin radiated from it ; in van Duyse's, in a pigeon, it measured 2.5 mm. The eyebrows were absent in two cases. The eyeball can always be felt under the skin ; it shows spontaneous movements, proving the presence of extrinsic muscles. There is evidence that the eye is always responsive to bright light, as shown by wrinkling of the skin ; this further proves the presence of the orbicularis.

In six cases the abnormality was bilateral, unilateral in three. Consanguinity in the parents has been recorded once only.

Other abnormalities are generally present, especially syndactylism (Manz, Chiari, Otto) and malformation of the genitalia (Manz, Chiari) ; meningo-encephalocele (van Duyse), hare-lip (Chiari), cleft palate, facial fissures, malformed concha, atresia of the larynx (Chiari), ventral hernia (Manz), aplasia of the kidneys, etc., have been observed.

The presence of orbicularis, levator palpebræ, and extrinsic muscles has been confirmed anatomically. It is not accurate to state that the lids are absent, since remnants were found by van Duyse and others. Bach alone found Meibomian glands and a tarsus in the upper lid. The raphe consisted of scar-tissue in Chiari's case, but only showed denser structure and aggregation of sweat-glands in van Duyse's. Usually the conjunctival sac is completely absent, but traces have been found.

The eyeball is invariably disorganised. The cornea is converted into vascular scar-tissue, often ectatic. The iris is adherent to the cornea, or more or less completely atrophied. The lens may be represented by only a few large vesicular cells behind the cornea or may have disappeared. The ciliary body and choroid show those changes familiar after severe inflammation, or are absent. The condition may be so extensive as to justify the term " cicatricial cryptophthalmia " (Wernicke).

The explanation of these abnormalities offers the usual difficulties. Manz considered that the lids were not formed (ablepharon by agenesis). There can be no doubt in some cases that the lids are partially formed and for some reason become united (ankylo-symblepharon by ankylosis).

The condition of the eye has been accounted for as a defective development of the lids and conjunctival sac; owing to the absence of lids the conjunctiva develops into skin (Treacher Collins); on this theory cryptophthalmia is the ultimate development of dermoid growth. Kundrat and van Duyse, again, have recourse to pressure by the amnion, and this is supported by the coincidence of syndactylism, but it is difficult to reconstruct the exact mode of action.

ZEHENDER.—K. M. f. A., x, 1872. HOCQUART.—A. d'O., i, 1881. CHIARI.—Prager Zeitschr. f. Heilkunde, iv, 1883. FUCHS.—Wiener klin. Woch., 1889. VAN DUYSE.—Ann. d'Oc., ci, 1889; Festschrift für van Bambeke, Bruxelles, 1889; A. d'O., xix, 1899. GILLET DE GRANDMONT.—A. d'O., xiii, 1893. *OTTO.—Wiener klin. Woch., 1893. BACH.—A. f. A., xxxii, 1895; A. of O., xxvii, 1898. KARMANN.—Arch. f. Kinderheilkunde, xviii, 1895. KUNDRAT.—Wiener klin. Woch., 1889. WERNICKE.—C. f. A., xxi, 1897. TREACHER COLLINS.—Lancet, 1900.

Microblepharon, ablepharon.—Various degrees of defective development have been recorded. Fuchs has described three cases of shortness of the lids, one of which was undoubtedly and the other two were probably congenital. Apart from the shortness, and consequent inability to close the lids, these were apparently normal.

The first case of true microblepharon was recorded by Friderici (1737); the rudimentary eyes were surrounded by nodules of skin, representing rudimentary lids (Cornaz). Seiler (1833) described a case in which a very prominent globe was surrounded by a circular fold of skin, scarcely 5 mm. high, the palpebral aperture measuring 24 mm. Gallenga (1892) has described two cases of microblepharon. The first occurred in a fœtus of eight months, with anencephaly and spina bifida. The lids were much reduced in size, especially on the temporal side. The second fœtus had an oblique facial fissure, and on the opposite side to the microblepharon total coloboma of the lower and partial coloboma of the upper lid.

FUCHS.—A. f. A., xv, 1885. FRIDERICI.—Monstra humana rariss., Lipsiæ, 1737. CORNAZ.—Des Abnormalities congénitales des Yeux, Lausanne, 1848. SEILER.—Beobach- tungen ursprüngl. Bildungsfehler der Augen, Dresden, 1833. GALLENGA.—Contrib. allo Studio di alcune Deform. congen. delle Palpebre, Torino, 1892; in Nagel's Jahresbericht, 1892.

Entropion.—Congenital entropion is excessively rare as an isolated phenomenon; it is somewhat commoner associated with epicanthus, and relatively frequent in microphthalmia and anophthalmia. In the latter both lids are affected, otherwise only the lower. Guibert attributes simple entropion to defective development of the tarsus. In Dimmer's case there was excessive development of skin.

DIMMER.—K. M. f. A., xxiii, 1885. GUIBERT.—A. d'O., xii, 1892. HARLAN.—T. Am. O. S., 1895.

Ectropion.—Congenital ectropion is also very rare. It is seen in the lower lid in the presence of orbito-palpebral cysts, the upper lid being then inverted. It has also been seen in microphthalmia (v. Ammon) and in buphthalmia (Marcus Gunn).

Trichiasis.—Stephenson has described trichiasis as a not uncommon congenital malformation. The condition occurred in two members of

the same family. The cases were probably slight examples of entropion, though it is definitely stated that the intermarginal zone was normally situated. Stephenson considers it due to incomplete development of the tarsus; if so, it is scarcely possible for it to arise with quite normal direction of the intermarginal strip. In Denig's case there was definite entropion of two-thirds of the upper lid.

STEPHENSON.—T. O. S., xiv, 1894. ISCHREYT.—C. f. A., xxii, 1898. DENIG.—Versamml. der deutschen Naturf. u. Aerzte zu München, 1899.

Distichiasis.—Distichiasis is a rare condition of which I have seen one case, involving all four lids. There is a regular, well-developed second row of cilia occupying the position of the orifices of the ducts of the Meibomian glands. Cases have been recorded by Becker, Herrnheiser, Zirm, Casey Wood (hereditary), Ischreyt, Westhoff (hereditary), Kuhnt and Erdmann (hereditary). Kuhnt examined the condition microscopically. The Meibomian glands were entirely absent and were replaced by the inner row of cilia, which, however, had sebaceous glands opening into the follicles. Moll's glands were hypertrophied, and there was a second row of Krause's glands in the middle of the tarsus. Kuhnt regards the condition as an heterotopic developmental anomaly. In Erdmann's cases Meibomian gland acini were present, and the ducts opened into the follicles of the anomalous cilia, exactly like normal sebaceous glands. The anatomical conditions were thus the same as in Herrnheiser's and Kuhnt's cases : it is merely a question of nomenclature whether the glands are called sebaceous or Meibomian.

BECKER.—Bericht ü. d. Wiener Universität, Wien, 1867. HERRNHEISER.—Prager med. Woch., 1891. ZIRM.—Wiener klin. Woch., 1892. CASEY WOOD.—Chicago Ophth. Soc., 1898. ISCHREYT.—C. f. A., xxii, 1898. WESTHOFF.—C. f. A., xxiii, 1899. *KUHNT.— Z. f. A., ii, 1899. STEPHENSON.—T. O. S., xxii, 1902. *ERDMANN.—Z. f. A., xi, 1904.

Conjunctival bridges.—Schapringer (1899) has described apron-like folds of conjunctiva on the inner surface of the normal upper lid as a congenital deformity (*angeborene Schürze, conjonctive en tablier, epitarsus*). The folds may be broad, *e. g.* 15 mm., diminishing towards the free edge of the lid, and a probe may be passed for some distance beneath them. Schapringer attributes them to adherence of the amnion to the circumocular tegument which subsequently forms the conjunctival surface of the lid. The same condition had been previously observed by Harlan and de Schweinitz in a child æt. 6 weeks, with congenital entropion. A large number of cases identical anatomically have been described by Herbert in Hindus, and attributed to conjunctival adhesions after neglected inflammation, especially trachoma. It is probable that the condition may be either congenital or acquired.

HARLAN AND DE SCHWEINITZ.—T. Am. O. S., 1895. SCHAPRINGER.—Z. f. A., ii, 1899 ; C. f. A., xxix, 1905. HERBERT.—T. O. S., xxi, 1901.

Ptosis.—This is a common congenital deformity : it is almost always bilateral, and usually incomplete. It is often hereditary, occurring in the males (Lawford, Vossius, Guende, Schiler, Gourfein), or in both sexes (Rampoldi, Heuck, Hirschberg, Vignes). It may be scarcely noticeable until the patient attempts to look up. Vicarious

contraction of the frontalis and elevation of the brow is only seen if the lid covers the pupil, and is then only developed as intelligence increases.

In simple, non-hereditary congenital ptosis there is usually defective movement of the globe upwards : this may be the result of disuse. Heuck states that the superior rectus is always present, though it may be inserted abnormally far back. Other defects of motility are also seen—*e. g.* of all the extrinsic muscles supplied by the third nerve (Tilley), all the extrinsic muscles (Uhthoff, Ahlström, Guende, Grauer, Gast, Schröder, Lucanus, Schiler, Hirschberg, Recken). It is noteworthy that the pupillary movements and accommodation are always normal. The facial innervation may be defective (Marina, Bach). There is generally strabismus, with congenital defects of movement of the external muscles. Vision is often subnormal, partly owing to congenital amblyopia (Bach and Lamhofer), partly to errors of refraction, especially astigmatism (Vossius). There is sometimes nystagmus. Other malformations are occasionally present, especially epicanthus (q. v.).

Hereditary congenital ptosis is almost invariably associated with other, usually extensive, defects of motility of the globe : 16 cases have been reported (*see* Wilbrand and Sänger). In all these cases pupillary movements and accommodation were normal.

Besides heredity, race has been incriminated as an ætiological factor ; thus Kunn observed congenital defects of the ocular muscles in 11 Jews out of 19 cases. Berger saw unilateral paralysis of the levator and superior rectus, and v. Michel unilateral ptosis as the result of delivery by forceps. In moderate degrees of congenital ptosis the lids may show movements on mastication, deglutition, etc. (synkinesis, or associated movement) (*cf.* Helfreich).

Points of diagnostic importance are the absence of secondary contracture, retention of convergence in the absence of lateral movements, absence of diplopia, presence of nystagmus, etc. Most of these apply to the associated bulbar paralyses.

Anatomically, congenital ptosis may be due to various conditions ; since they apply equally to defects of movement of the globe examples of these also may be given here.

(1) Defective development of the muscle. Lawford, in a man with congenital deviation of the eyes to the right, on *post-mortem* examination found absence of the right internal rectus and very slight development of the left external. Heuck found a very poor levator, only 2 mm. broad, in a case of congenital ptosis. Bach saw in a case slight development of the levator with moderate atrophy of the superior rectus, whilst the third nucleus was normal.

(2) Bifurcation of the muscle. This has been seen by Dieffenbach in the internal rectus in congenital convergent strabismus.

(3) Defective separation of muscles. Morgagni saw union of the superior oblique with the trochlea. Olbers and Wrisberg found on the right side fusion of the superior and external recti and on the left of the superior oblique and the internal rectus : in another case the levator palpebræ and superior rectus were fused, as well as the external with the inferior recti and the internal rectus with the superior oblique.

(4) Abnormal insertion of muscles. Examples are recorded by Rossi, Dieffenbach, Pflüger, Heuck, and others. In Heuck's case all the muscles except the two internal recti were mal-placed. The superior, inferior, and external recti were inserted too far back, sometimes as much as 2·5 mm. Each superior oblique was inserted to the nasal side of the corresponding superior rectus.

(5) Muscles replaced by fibrous strands. This was the case in the levator in an example of congenital ptosis reported by Ahlström. Uhthoff once found the rectus internus as a normally inserted fibrous band and Baumgarten the rectus externus.

(6) Complete absence of the muscle. In Lawford's case the internal rectus was absent; in Ahlström's and Heuck's, the levator; in Harles's, both obliqui; in Seiler's, the right superior rectus and both inferior obliques; in another case both right obliques and the left superior rectus and both obliques; in Steinheim's, the superior rectus.

(7) Defective development of the nerves. Cornaz refers to a case observed by Cerutti of hydrocephalus with microphthalmia in which the third, sixth, and first branches of the fifth nerve were mere fibrous cords.

(8) Absence of the nerves. Seiler observed three cases in which various nerves were absent. In one, with hydrocephalus and microphthalmia, the ciliary ganglion and its branches, the lacrymal branch of the fifth, and all the ocular nerves except the sixth were absent; in another, with hydrocephalus, all the nerves on the right side and the left fourth, first branch of the fifth, and parts of the third were absent.

(9) Aplasia or agenesis of the nuclei of the nerves. Wilbrand and Sänger examined a case of bilateral congenital ptosis in a man, æt. 47, who died of phthisis, and found almost complete aplasia of the large-celled lateral group of the right third nucleus and a slighter degree of aplasia of the opposite Westphal-Edinger group. The observation is further of great neurological interest, since it points to an innervation of the levatores palpebrarum resembling that involved in hemianopsia.

It is important to remember the fact demonstrated by Leonowa and others that the voluntary muscles develop in early foetal life quite independently of the anterior horn nuclei, so that defective mobility may ensue from absence or aplasia of the nuclei, from defect or absence of the muscles, or from defect or absence of the conducting paths (Wilbrand and Sänger).

LAWFORD.—T. O. S., viii, 1888. VOSSIUS.—B. z. A., v, 1892. GUENDE.—Rec. d'O., 1895. SCHILER.—Correspondenzbl. Württemberg. Aerzte, 1895. GOURFEIN, C. f. A., xx, 1896. RAMPOLDI.—Ann. di Ott., xvi, 1887. HEUCK.—K. M. f. A., xvii, 1879. HIRSCHBERG. —Neurol. Centralbl., iv. VIGNES.—Rec. d'O., 1889; Soc. d'Ophth. de Paris, 1889. TILLEY. —Gaz. hebdom., 1886. UHTHOFF.—Jahresbericht d. Schöler'schen Augenklinik, 1881, Berlin, 1882. AHLSTRÖM.—B. z. A., xvi, 1895. GRAUER.—In Nagel's Jahresbericht, 1889. GAST.—K. M. f. A., xxvii, 1889. SCHRÖDER.—Bericht ü. d. Augenklinik Nerothal. Wiesbaden, 1872. LUCANUS.—K. M. f. A., xxiv, 1886. RECKEN.—K. M. f. A., xxix, 1891. MARINA. — Ueber multiple Augenmuskellämungen, Leipzig u. Wien. BACH.—Centralbl. f. Nervenh. u. Psych., 1893. BACH AND LAMHOFER.—Möbius neurol. Beiträge, iv. KUNN. —B. z. A., xxvii, 1898. BERGER.—A. f. A., xvii, 1887. v. MICHEL.—In Nagel's Jahresbericht, 1887. HELFREICH.—B. d. o. G., 1888. HEUCK.—K. M. f. A., xviii, 1880. BACH. —A. f. A., xxxii, 1895. DIEFFENBACH. — Das Schielen, Berlin, 1842. PFLÜGER.— K. M. f. A., xiv, 1876. STEINHEIM.—K. M. f. A., xv, 1877. LEONOWA.—Neurol. Centralbl., xii. *WILBRAND AND SÄNGER.—Die Neurologie des Auges, Wiesbaden, 1900.

Epicanthus.—Schön (1828) first described a semilunar fold of skin situated at the inner angle, and considered it to be a vestigial supplementary eyelid. v. Ammon (1841) called it epicanthus, and attributed it to excessive development of skin at the root of the nose. The fold is crescentic, with the concavity outwards, and varies in size, sometimes covering the inner canthus and even a considerable part of the globe. Usually the neighbouring parts are normal, but in v. Forster's case the caruncle was absent. Epicanthus is nearly always bilateral, though v. Ammon's case was unilateral, and it is often unequally developed on the two sides. The eyes are abnormally wide apart, the nose being flattened. It often disappears as the nose develops, but when continued into adult life there is frequently not only an apparent, but also a real, convergent strabismus, and ptosis (Hirschberg, Möbius, Schmidgall, Bach, v. Forster, Vignes) and defective mobility of the eyes, especially upwards, are not uncommon (v. Graefe). v. Graefe was therefore inclined to attribute the condition to insufficiency of branches of the oculomotor nerve. Bach, in one slight case, found very deficient development of the levator and superior rectus.

Epicanthus is not infrequently congenital ; Manz reported five cases from v. Graefe's clinic in brothers and sisters, whilst the other five children were free from the defect. Steinheim records a remarkable series of 18 cases in various members of one family. It has been attributed to atavism, since it is normal in Mongolian races which have low nasal arches. Manz considered the condition due to the defective development of the bones of the nose and orbit : E. v. Hippel points out that this is an assumption, and thinks that epicanthus is due merely to excessive development of skin.

de Wecker and Martin report associated microphthalmia, and de Wecker also "lacrymal tumours." Sichel and Chevillon described cases of external epicanthus—*i. e.* at the outer canthus ; it is doubtful if the analogy of the two conditions is justifiable.

Schön.—Handbuch d. path. Anat. d. Auges, 1828. v. Ammon.—v. Ammon's Zeitschrift, i, 1831. v. Forster.—Münch. med. Woch., 1889. Hirschberg.—Neurol. Centralbl., iv. Schmidgall.—Dissertation, Stuttgart, 1895. Vignes.—Rec. d'O., 1889. Bach.—A. f. A., xxxii, 1895. Manz.—In G.-S., ii, 1876. Steinheim.—C. f. A., xxii, 1898. de Wecker.—Études ophthalm., i, Paris, 1853. Sichel, Chevillon.—Ann. d'Oc., xxix, 1853.

Elephantiasis neuromatodes.—*See* Vol. I, p. 13 ; Vol. II, p. 730.
Nævi.—*See* Vol. I, p. 28.
Dermoids.—*See* Vol. I, p. 29.
Dermoid cysts.—*See* Vol. II, p. 716.

The Conjunctiva.

Pigmentation.—*V. infra*, "Anomalies of Pigmentation."
Pterygium.—*V. supra*, p. 776.
Congenital tumours.—*See* Vol. I : Nævus, p. 127 ; Epithelial Plaques, p. 130 ; Dermoids, p. 132 ; Dermo-lipomata, p. 135 ; Osteomata, p. 137.

The Cornea.

Congenital opacities.—Klintosch (1760) first described congenital opacities of the cornea: Farar (1790) saw progressive recovery in three brothers. Other cases were reported by Mayor (1808), Beer (1813), Ware (1814), and v. Ammon (1830) first seriously discussed the subject, being followed by Middlemore (1835), Cornaz (1848), and Fronmüller (1855).

Congenital opacities may be partial or complete, permanent or transitory. They may be associated with modifications in the curvature or with more extensive lesions—*e. g.* anterior synechiæ, anterior staphyloma (q. v.), colobomata of the iris and choroid, dermoids, microphthalmia, etc.

Arcus or annulus juvenilis (Wilde), embryotoxon (v. Walther), fœtal arcus (v. Ammon), or macula arcuata (Sybel, 1799) is a condition anatomically exactly resembling complete arcus senilis, having the same ring of almost clear cornea external to it. Landesberg recorded a case in a child æt. 17 days, the mother having the same anomaly. The condition has been attributed to arrested development, though such a stage has not been observed embryologically. A case of annular opacity in the deepest layers of the cornea, with annular adhesion of the iris and pupillary membrane in both eyes, tends to throw some light upon the subject. The author, Maager, attributed it to arrested development, but it is more reasonably explained as a result of fœtal inflammation (E. v. Hippel).

Tongue-shaped opacities at the periphery, exactly resembling those commonly found in sclerosing keratitis, also occur congenitally; they may be thin and diffuse or very dense; they are usually permanent. Talko records such a case in a microcornea with iris synechia outwards in the other eye, talipes, and left hemiplegia; the patient died of hydrocephalus.

A considerable number of cases of congenital nebulæ or leucomata have been published, some situated near the margin, others near the centre. Of the former that of Landesberg in the upper nasal quadrant, raised above the normal level, may be mentioned, as well as those observed in animals by Schulteiss and Rückert. Vossius, in a girl æt. 9, saw a small leucoma near the outer margin, associated with aniridia in the other eye. Central opacities have been reported by Steffan, Frohmüller, and others. General dense opacity is common in microphthalmia, and some opacity is not very rare in buphthalmia (q. v.) (*e. g.* Marcus Gunn).

The cases of adherent leucoma, such as that recorded by Landesberg, form an intermediate group leading on to the congenital anterior staphylomata.

As regards the cause of congenital corneal opacities the two theories of arrested development and intra-uterine inflammation have been evoked. Most authors accept the latter theory, which is so strongly supported by some of the cases of anterior staphyloma (q. v.). The same arguments apply to adherent leucomata, though these may be explained with some show of reason as cases of defective separation

of the iris from the cornea (see "Anterior Synechiæ"). The length of time that the cornea remains opaque normally in fœtal life is not satisfactorily determined (E. v. Hippel), but it is definitely proved that it is at no time vascularised, with the exception of the narrow rim at the limbus, as in the adult (Leber, Schöbl). The vascularisation and infiltration which are found in congenital opacities must therefore be of inflammatory origin. Treacher Collins has recently recorded two cases æt. 7 and 3½ respectively with vascularisation in the same family, but he does not accept the inflammatory theory. The theory of incomplete differentiation of the mesoblast lying between the cornea and the lens involves a much less trustworthy assumption.

KLINTOSCH.—In Picqué, Anomalies de Développement, etc., Paris, 1886. FARAR.—Med. Commentaries, ii, 1790. MAYOR.—Thèse de Montpellier, 1808. BEER.—Das Auge, Wien, 1813. WARE.—Remarks on Ophthalmy, London, 1814. v. AMMON.—v. Ammon's Zeitschrift, 1830. MIDDLEMORE.—Treatise, 1835. FRONMÜLLER.—Ann. d'Oc., xxxviii, 1857. LANDESBERG.—K. M. f. A., xxiv, 1886. MAAGER.—Wiener klin. Woch., 1895. TALKO.—K. M. f. A., xiii, 1875. SCHULTEISS, RÜCKERT.—Z. f. vergleich. Augenhkde., iii, 1885. VOSSIUS.—K. M. f. A., xxi, 1883. STEFFAN.—K. M. f. A., v, 1867. MARCUS GUNN. —T. O. S., xviii, 1898. LEBER.—Anat. Untersuchungen. Wiener Akad., 1868. SCHÖBL.—C. f. A., x, 1886. TEPLJASCHIN.—A. f. A., xxx, 1895. HILBERT.—Virchow's Archiv, cxxxi; K. M. f. A., xxx, 1892. BAAS.—C. f. A., xviii, 1894. BRAUN.—Dissertation, Heidelberg, 1895. TREACHER COLLINS.—T. O. S., xxv, 1905. PETERS.—K. M. f. A., xliv, 1906.

Anterior staphyloma.—Very few cases of congenital anterior staphyloma are on record. Of these, the first four may be dismissed briefly; they are incompletely reported, and were not examined microscopically.

Beer (1813) describes a child with congenital abnormalities in both eyes; in the left the lids were united along their whole length, and on separating them the cornea was seen to be pearly white. It may have been a case of cryptophthalmia.

Schön (1828) mentions that v. Ammon gave notice of a case of congenital staphyloma to a medical society, but it does not appear to have been actually brought forward.

Sonnenmayer (1839) mentions that Sichel saw a case of congenital staphyloma of the cornea, half an inch high; he states that "it is certain that the eye has undergone phlogistic processes during uterine life."

Crompton (1840) describes two brothers with congenital opacities of both corneæ, the left eyes in each case being staphylomatous. He confines his remarks chiefly to the opacities.

Krückow (1875) reports two cases. The first was not a true staphyloma, but a congenital opacity with an iris cyst. The second was a boy, æt. 11, with right anterior staphyloma and left microphthalmia, both dating from birth. The right eye was excised; it measured 23·5 mm. in ant.-post. diameter. The staphyloma was very thin, and showed traces of earlier perforation in the lower outer quadrant. The corneal stroma was slightly infiltrated with lymphoid cells. Descemet's membrane was absent; the back of the cornea was lined with iris pigment. Lens absent. Retina—fibrous degeneration. Optic nerve—partial excavation (v. p. 792).

Treitel (1876) described another case. The globe was enlarged, the

cornea hemispherical and thickened in the staphylomatous part. Bowman's and Descemet's membranes had disappeared; the cornea was lined with atrophic iris. The cataractous lens lay on a pigmented fibrous mass behind the cornea. Retina—atrophy of ganglion-cells and nerve-fibre layer. Choroid—poor in pigment, thinned and infiltrated in the anterior part. Optic nerve—deep triangular excavation (? physiological), nerve-fibres degenerated.

Schiess-Gemuseus (1884) reported the case of a girl, æt. 2½, whose L. eye was white and prominent from birth. The globe was enormously enlarged; sagittal diameter 32·2 mm., vertical and horizontal diameter 24·9 mm. The cornea was much thickened, vascularised, and infiltrated, the deeper layers consisting of scar-tissue. The parenchyma contained masses of brown pigment. Descemet's membrane was

FIG. 550.—CONGENITAL ANTERIOR STAPHYLOMA.

Parsons, T. O. S., xxiv. Outer portion of the eye, slightly magnified.

FIG. 551.—CONGENITAL ANTERIOR STAPHYLOMA. × 2.

From the same specimen. Sagittal section.

present only at the periphery. Remains of the atrophied iris were adherent to the back of the cornea, and behind this was a dense white mass of fibrous tissue containing lens capsule. The ciliary body was atrophic; the optic disc was not cupped.

Hirschberg and Birnbacher (1886) recorded the case of a girl, æt. half an hour, born four weeks before term, with right anterior staphyloma and left phthisis bulbi. The right globe was excised four hours after birth. The staphyloma formed a blackberry-like mass, consisting of true cornea at the sides, where Bowman's and Descemet's membranes were intact for a short distance. In front there was a pseudo-cornea of scar-tissue, with flat cells, covered only partially with epithelium. The iris lined the staphyloma. The lens was shrunken (2·6 mm. in diameter) and globular, the ciliary body flattened and atrophic.

Bernheimer (1887) described a very rare case belonging to a somewhat different category. A girl, æt. 6 months, had an anterior staphyloma consisting of dermoid tissue, with hair-follicles and sebaceous glands. Even in this case Descemet's membrane was absent over a certain area, the ends being rolled forward in the usual manner. The iris was completely adherent to the cornea. The lens was *in situ*. The case may be compared with other teratoid developments in the front of the eye (*cf.* Cohn[1]) and with cryptophthalmia.
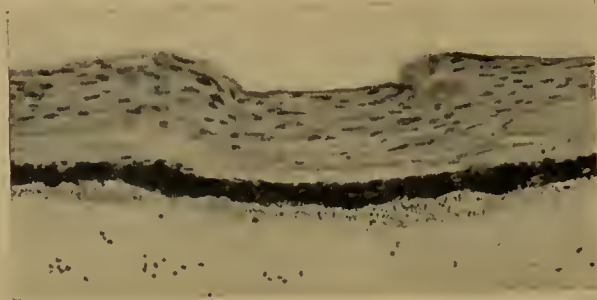
FIG. 552.—CONGENITAL ANTERIOR STAPHYLOMA. × 120.
From the same specimen. Anterior part of pseudo-cornea.

Pincus (1887), in a dissertation on congenital anterior staphyloma, described an eye from a 10 months child, with a staphyloma dating from birth. The pseudo-cornea was thick, covered with thickened epithelium, and consisting of dense scar tissue, vascularised in the superficial layers. Bowman's membrane was absent, and Descemet's present only at the periphery. The atrophic iris was almost entirely fused with the pseudo-cornea. The lens capsule lay in a mass of
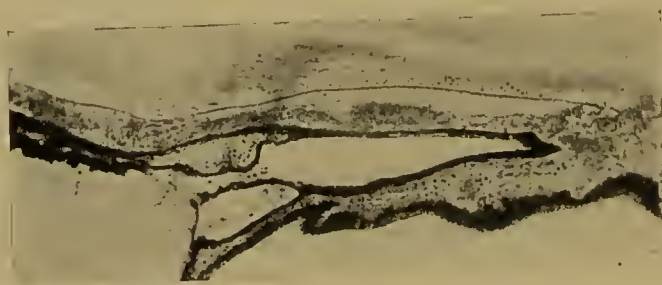
FIG. 553.—CONGENITAL ANTERIOR STAPHYLOMA. × 55.
From the same specimen. Descemet's membrane at periphery of cornea, breaking up anteriorly.

fibrous tissue stretching from the middle of the cornea to the shrunken vitreous.

Steinheim (1897) gave an account of an extraordinary family, which he apparently attended and had ample opportunities of investigating. The children were as follows: (1) boy, æt. 6, both eyes staphylomatous; (2) girl, æt. 5, eyes normal; (3) girl, æt. 4, right eye total staphyloma, left eye small with cystic ectasia; (4) girl, æt. 3, both eyes total

[1] COHN.—Inaug. Dissert., Heidelberg, 1897; see 'Graefe-Saemisch,' 2nd edition, Lfg. 18 and 19, 1900.

staphyloma; (5) boy, æt. 2 months, both eyes white and shrunken. The last child was seen when 14 days old, when both eyes were white and prominent. There was no microscopical investigation. In no case was there inflammation or purulent discharge at birth.

Westhoff (1899) briefly reported the case of a girl, æt. 1 day, born after prolonged labour (breech presentation). The right eye was shrunken, with opaque cornea; the left had an anterior staphyloma. There was no discharge.

Runte (1903) exhaustively reports a recent case. The child was seen when it was half a day old. The staphyloma commenced to ulcerate, and the eye was excised on the fourth day. It was 22½ mm. long, the staphyloma forming 8 mm. This varied from ½ to 1 mm. thick, the central part being devoid of epithelium. The corneal tissue

FIG. 554.—CONGENITAL ANTERIOR STAPHYLOMA. × 60.
From the same specimen. Periphery of cornea, showing termination of epithelium and dense infiltration of substantia propria.

had almost entirely disappeared, being replaced by scar-tissue, containing many pus-cells and lymphocytes. The posterior layers were formed of denser fibrous tissue. There were numerous blood-vessels. Bowman's and Descemet's membranes were absent. The staphyloma was lined with iris pigment, which also invaded the scar in parts. The posterior chamber contained fibrinous coagulum with pus-cells, which also lay between the ciliary processes. The lens was dislocated and cataractous, the capsule being intact. The retina and choroid showed no striking pathological changes. The optic disc was not excavated.

I have examined one case, which may be recorded here in detail.

Ethel C—, æt. 3 days, was admitted to the Royal London Ophthalmic Hospital on November 11th, 1903, with an anterior staphyloma. The condition was noticed at birth. The mother was healthy. The

confinement was normal, no instruments were used, and the child was born immediately after the rupture of the membranes. There was one other child, æt. 9, who had no deformity.

The child was otherwise normal. Right eye normal.

Left eye.—There was a very slight mucous discharge. The globe showed a complete anterior staphyloma, projecting half an inch beyond the lids. No a. c.; iris adherent to pseudo-cornea, which was very thin and almost transparent. The pupil could be made out, and the iris tissue was most stretched in the lower part, where it gave somewhat the appearance of a coloboma. Careful examination showed striations of pigment over this area.

Bacteriological examination.—Films from the conjunctiva showed cocci, positive to Gram ; culture showed *Staphylococcus albus.*
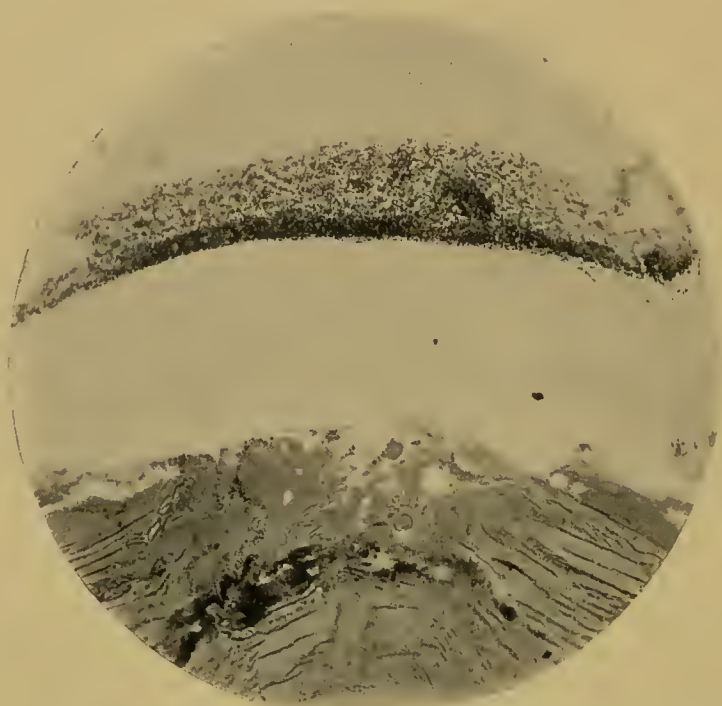
FIG. 555.—CONGENITAL ANTERIOR STAPHYLOMA.   × 55.
From the same specimen. Anterior pole of lens, showing ruptured and convoluted capsule and anterior polar cataract.

The eye was excised the same day. It was somewhat hour-glass shaped. Antero-posterior diameter, 22 mm. ; transverse and vertical, 12 mm. The anterior staphyloma measured 10 mm. from anterior pole to groove on sclerotic.

The eye was hardened in 10 per cent. formol, and divided in a sagittal direction to the outer side of the nerve.

Macroscopic examination.—There was a large anterior staphyloma forming rather more than a hemisphere. The anterior part was extremely thin, composed of iris, covered by a transparent membrane. The sides were thicker and opaque, consisting of cornea, lined by iris, which was completely adherent. The posterior chamber contained masses of yellow inflammatory material. The lens was *in situ,* on a

level with the ciliary body, which corresponded with the external sulcus, into which the lids fitted. The retina and choroid were *in situ*; the vitreous contained yellow material.

Microscopic examination.—The cornea at the sides consisted of well-marked substantia propria, covered with stratified epithelium. The interlamellar spaces were packed with polymorphonuclear leucocytes, which also invaded the epithelium. Bowman's membrane was absent everywhere. Descemet's membrane was intact on each side for a distance of 1 mm. The epithelium persisted for 2 to 3 mm. in front of the sulcus, and then suddenly stopped. The substantia propria was densely infiltrated in front of this, and quickly narrowed to a thin membrane. As it narrowed the posterior part was most infiltrated, the anterior being homogeneous, except for a few rod-like nuclei; these, seen on the flat, were oval. The thin membrane which formed the whole of the dome-shaped projection consisted of several layers of these cells, without any epithelium on the surface. Internal or posterior to these layers was an almost homogeneous layer of about one third to half the thickness, showing only faint striations. Internal to this was the iris, reduced to rarefied and distorted retinal pigment epithelium.

The large posterior chamber contained a fibrinous coagulum, richly infiltrated with polymorphonuclear leucocytes.

The lens was in its normal position. Its thin anterior capsule was ruptured in all the mesial sections, and lay somewhat separated from the cortex, forming a hyaline wavy line, covered by polymorphonuclears. The anterior capsular epithelium was absent at and for a short distance around the anterior pole; elsewhere the capsule adhered to the cortex, and the cells were well formed at the equator. The cortex was broken up and cataractous at the anterior pole; there was no evidence of anterior capsular cataract. The cortex was also cataractous at the equator and posterior parts. An important point was the presence in some sections of polymorphonuclears between the cortical fibres at the anterior part.

The ciliary body was infiltrated, engorged with blood, and detached posteriorly. The ciliary processes were drawn inwards towards the lens and stretched.

The vitreous was permeated with fibrinous coagulum, containing polymorphonuclears, especially aggregated on the retina in the lower part and on the optic disc.

The retina was inflamed and moderately infiltrated; the layers were well maintained, even the rods and cones being for the most part intact. It was *in situ*, though slightly folded—probably an artefact.

The choroid was intensely congested, and diffusely infiltrated with leucocytes. The pigment was as yet undeveloped. The demarcation between choroid and sclera was indistinct, but the choroid was detached anteriorly, the subchoroidal space containing coagulum.

The optic nerve was densely infiltrated with polymorphonuclear leucocytes; the vessels were widely dilated and packed with red corpuscles. Nettleship has since published two other cases.

Congenital anterior staphyloma is probably the most conclusive

proof of the effects of intra-uterine inflammation which is at present available. The question has already been discussed (*v.* p. 772).

A remarkable case published by Arnold Lawson and Coats gives an example of very rare anomalies in the uveal tract, such as have, however, been observed once before, viz. in one of Krückow's cases. In it Descemet's membrane is absent for the most part. The intercalary region is much expanded, so that the distance from the limbus to the anterior end of the ciliary muscle is much increased. The cornea is much thickened except in the centre, corresponding with the pupil, the iris not being adherent here. In this situation a piece of lens capsule (Fig. 556, L. C.) is intimately adherent to the posterior surface, with some rounded masses of lens substance (L. S.). The iris

FIG. 556.—CONGENITAL ANTERIOR STAPHYLOMA.
Arnold Lawson and Coats, T. O. S., xxvi. See text.

is adherent to the cornea over almost the whole of its area. It is thinned, much stretched, and considerably atrophied, but its pigmented layers are intact and the sphincter is practically unaltered. In the periphery on one side there is an area over which the iris is not adherent (Fig. 557, A). Here there is a minute anterior chamber, the iris stroma is normal, and Descemet's membrane, with its endothelium, is easily recognisable. The ciliary processes commence immediately behind this area: they are greatly elongated, drawn forwards, and flattened against the iris (Fig. 557, C. P.). On the processes are very numerous cysts (c) formed by separation of the unpigmented from the pigmented epithelium. Following the uveal tract backwards, the pars plana (P. P.) is normal, and at about the usual distance behind the ora serrata is found. *Behind* this, again, the ciliary muscle (M. C.) is

seen, with a large artery, the circulus iridis major (C. I. M.) among the anterior fibres. The canal of Schlemm (C. S.) is situated slightly behind the anterior end of the ciliary muscle, and therefore considerably behind the ora serrata. It will be noticed that the relation of the various parts of the cornea-sclerotic are normal, as are, in less degree, the various parts of the uvea, but the two sets of structures are dislocated with regard to each other.

Only two cases, each in congenital anterior staphylomata, have
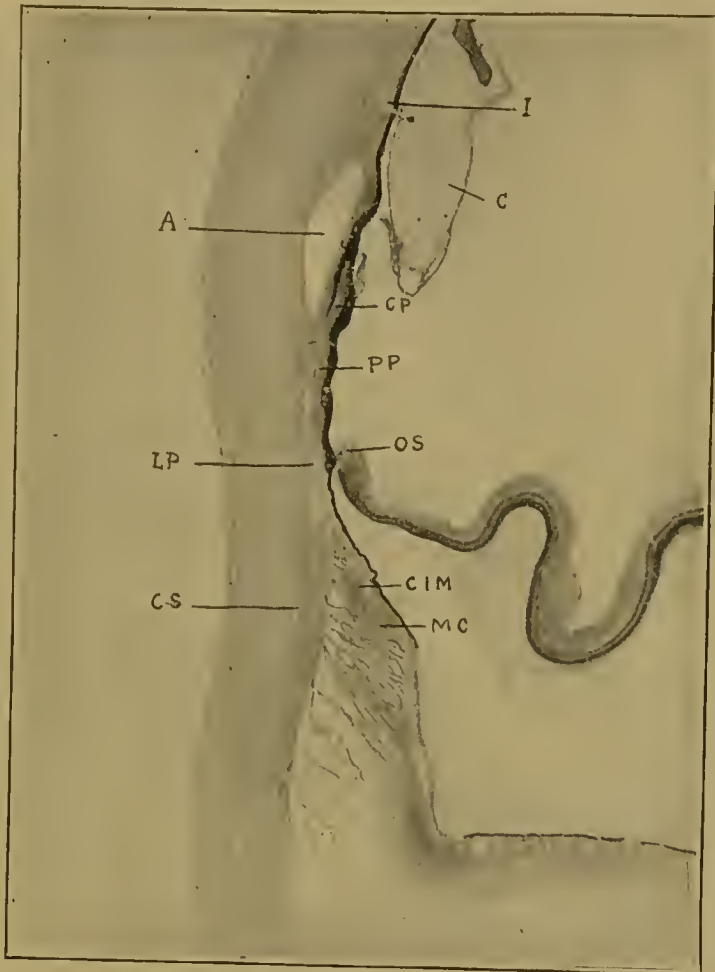
FIG. 557.—CONGENITAL ANTERIOR STAPHYLOMA.
Arnold Lawson and Coats, T. O. S., xxvi. See text.

been recorded of this anomalous arrangement. It is probable that the connection between the uvea and the structures external to it, including the ciliary muscle, is much looser in pre-natal life than subsequently : hence the absence of such a deformity in ordinary cases of anterior staphyloma. The ciliary muscle has a firmer attachment to the sclera than any other part of the uveal tract, and is therefore not displaced with it. In this connection it is interesting that in many lower animals, especially in birds, the relation between the inner layers of the uvea and the ciliary muscle is much less intimate than in man. The ciliary muscle practically belongs to the sclerotic and is attached

to the uvea only at its posterior end. Exactly those layers which in the bird are separate have been displaced forwards in these anomalous cases.

BEER.—Das Auge, Wien, 1813. SCHOEN.—Handb. der path. Anat. des mensch. Auges, Hamburg, 1828. SONNENMAYER.—Die Augenkrankheiten der Neugeborenen, Geln-hausen, 1839. CROMPTON.—London Medical Gazette, 1840. KRÜCKOW.—A. f. O., xxi, 1, 1875. TREITEL.—A. f. O., xxii, 1, 1876. SCHIESS-GEMUSEUS.—A. f. O., xxx, 1, 1884. HIRSCHBERG AND BIRNBACHER.—C. f. A., x, 1886. BERNHEIMER.—A. f. A., xviii, 1887. PINCUS.—Inaug. Dissert., Königsberg, 1887. STEINHEIM.—C. f. A., xxi, 1897. WESTHOFF. —C. f. A., xxiii, 1899. RUNTE.—A. f. A., xlviii, 1903. *PARSONS.—T. O. S., xxiv, 1904. NETTLESHIP.—Lancet, 1880 ; T. O. S., xxiv, 1904. A. LAWSON.—T. O. S., xxv, 1905. *A. LAWSON AND COATS.—T. O. S., xxvi, 1906.

Interstitial keratitis.—Some congenital opacities exactly resemble those of interstitial keratitis, and run a course which supports the contention that they are of identical nature and ætiology. The opacities are diffuse or localised, faint or very dense. They are specially interesting in that they clear up after birth, usually from the periphery towards the centre. Cases have been reported by Baas, Saltini, Barabaschew, Haensell, E. v. Hippel, Hosch, and others. It has not always been possible to establish a syphilitic history, and possibly some belong to the group of intra-partum opacities (*see* Vol. IV). The changes are deep seated, involving the part of the cornea derived from the uvea ; this is shown by staining on prolonged instillation of fluorescein (E. v. Hippel). In this respect they fall into line with the ordinary specific interstitial keratitis. There may be coincident coloboma of the choroid (E. v. Hippel). In Hosch's case no trace of anterior lens capsule could be found.

BAAS.—K. M. f. A., xxi, 1883. SALTINI.—Boll. d'Oc., x, 1888. BARABASCHEW.— Clinique opht., 1896. *HAENSELL.—T. Am. O. S., 1898. E. v. HIPPEL.—B. d. o. G., 1898 ; A. f. O., xliv, 3, 1895 ; lii, 3, 1901 ; liv, 3, 1902 ; Festschrift f. v. Hippel. Halle, 1899. HOSCH.—A. f. O., lii, 3, 1901.

Megalocornea, or keratoglobus, is found in buphthalmia (hydro-phthalmia, megalophthalmos). This is a condition of congenital glaucoma, and will be best discussed in connection with that subject.

Microcornea is found in microphthalmia. It requires no special consideration.

Keratoconus, or conical cornea. This is probably a congenital abnormality in some cases, though possibly not in all, since it may not become manifest until adult life. The evidence as to its ætiology is so scanty that it is at present futile to discuss it (*see* Vol. I, p. 174).

Additional References.—NOYES.—Internat. Congress, 1876. HIGGENS.—Lancet, 1884. RAMPOLDI.—Ann. di Ott., xvi, 1887. HIRSCHBERG —C. f. A., 1891. BULLARD.—Amer. Jl. of O., 1897. DESPAGNET.—Ann. d'Oc., cxvii, 1897. BAUMANN.—Dissertation, Erlangen, 1898. HARLAN.—Ophth. Rec., 1898. WAGENMANN.—A. f. O., xlvi, 1898. KELLY.— Ophth. Rec., 1900. PLAUT.—K. M. f. A., xxxviii, 1900. CALLIES.—Dissertation, Rostock, 1901. BUCHANAN.—T. O. S., xxiii, 1903.

Dermoid and teratoid tumours.—*See* Vol. I, p. 258.

THE IRIS.

Persistent pupillary membrane.—Between the second and third months of fœtal life the secondary optic vesicle becomes differen-

tiated into three segments : a posterior, optic, giving rise later to the retina proper ; an intermediate or ciliary ; and an anterior or iridic. The iridic segment, forming the lip of the optic cup, is at first very small, and consists merely of the two layers of epithelium. It gradually grows forwards, insinuating itself between the cornea and lens. Mesoblastic tissue becomes organised upon its anterior surface, giving rise to the stroma of the iris. The mesoblast which forms the cornea is at first in contact with the lens, but as early as the sixth week (Jeannulatos) a frontal cleft commences to separate it into two portions, thus forming a potential anterior chamber. The anterior part forms the cornea, the posterior the iris stroma and the anterior vascular sheath of the lens or pupillary membrane ; these remain in contact for a considerable period. At four months the anterior chamber is lined
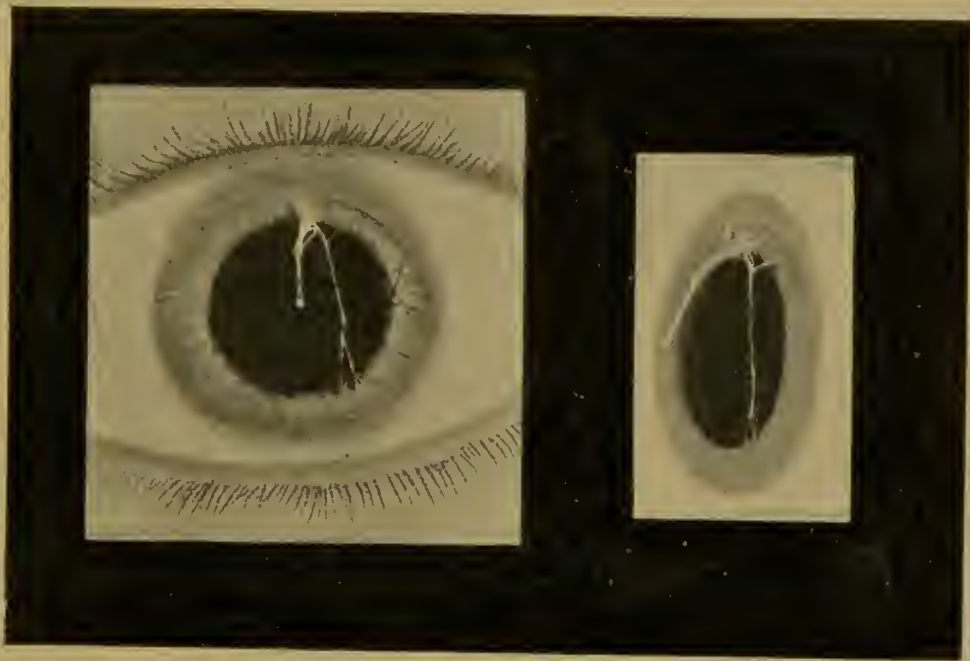
FIGS. 558 AND 559.—PERSISTENT PUPILLARY MEMBRANE.
Silcock, T. O. S., xv. Fig. 558, from in front. Fig. 559, from side, showing anterior synechia.

with endothelium. At about the middle of the seventh month the pupillary membrane commences to become absorbed.

The structure of the fœtal pupillary membrane is of some importance. According to v. Michel it consists of a finely granular membrane with diffuse oval nuclei. The anterior surface is covered with endothelium : the vessels are posterior and consist of endothelial tubes. According to Rumschewitsch the vessels have also an adventitia : the cells are long, spindle-shaped, and few in number, chiefly applied to the vessels. The membrane itself is structureless, with a few cells resembling leucocytes, and there are a few pigment-cells, but only near the iris.

The vessels of the anterior vascular sheath of the lens communicate with those of the posterior by the capillary equatorial zone, but the two

circulations are essentially distinct. Hence the pupillary membrane may persist whilst the posterior sheath entirely disappears.

The first exact description of a persistent pupillary membrane was furnished by Adolf Weber (1861). He pointed out as the essential diagnostic feature that the strands invariably arise from the anterior surface of the iris, generally in the position of the circulus arteriosus minor, but never from the pupillary margin. They often arise much peripheral to the lesser circle, even as far as the ciliary root.

The disposition of the fibres varies very much in different cases, and even in the same case in different conditions of constriction or dilatation of the pupil. The following arrangements have been met with: (1) several fibres arising at different points of the lesser circle stretch across the pupil and form a delicate network; the arrangement may resemble that of the vessels of the foetal membrane (van Duyse); (2) fibres run tangentially between two points on the lesser circle; (3) all the toothed projections of the small circle are prolonged inwards and project beyond the pupillary margin; (4) the fibres float free at their inner extremities; (5) loops are formed by pairs of fibres in front of the pupil; (6) a network of fibres unites in the pupillary area into a membranous plaque; (7) fibres are adherent at their inner extremities to the lens, with or without the formation of a plaque, or the presence of an anterior capsular cataract (capsulo-pupillary membrane); (8) fibres are adherent to the back of the cornea (anterior synechia of pupillary membrane). Mayerhausen described a very unusual form in which a dense membrane, springing from the lesser circle, covered nearly the whole pupil; indeed, on strong constriction the pupil disappeared behind it.

The fibres vary much in thickness; they may be so attenuated as to be only visible with high magnification. They may be grey and paler than the iris, or have the colour of the iris stroma. They are very extensile and do not impede the pupillary movements. Central capsular plaques are usually pigmented (Weber, Keyser, Arlt, Becker, Korn, Hirschler, and others), but not invariably. It is possible that the fibres may become absorbed in post-natal life; Stephenson is of the opinion that this does not occur. The filaments may be rudimentary, yet associated with pigmented deposits on the anterior capsule (Schleich, Franke). The spots are brown, round or angular or rod shaped. Schubert, by high magnification, found these spots in a large proportion of cases—33 per cent. in 1200 cases; they occurred chiefly in brown eyes, and in 4 per cent. fine filaments traversed the pupil. Mayerhausen found crystals of hæmatoidin in the rabbit.

The condition is generally uniocular. As regards frequency statistics vary: Mooren, 14 in 100,000: Uhthoff, 6 in 10,000; König-stein, 21 in 300 newborn; Schleich, 13 in 150. Franke found 32 in 3508; in 18 filaments were present, and in 14 a membrane; 3 cases had remnants in both eyes; the right and left eyes were affected in the proportion 7 to 5; and the sex ratio was 19 female to 13 male. Stephenson found vestiges in 68 cases out of 3414; in 13 both eyes were affected; the right and left eyes were affected in the proportion 25 to 17; the percentage in 1994 males was 1·81, in 1420 females 2·25.

Vision is not usually affected, though astigmatism is unduly common (32·5 per cent., Franke). A dense central plaque may seriously affect sight, so that operative measures are indicated (A. Graefe, Cohn, v. Hasner, Wicherkiewicz, Rumschewitsch, van Duyse).

Pyramidal cataract is rare : persistent posterior lens sheath is very rare (Mayerhausen, Franke, Berger). Other concomitant congenital lesions are aniridia (Treacher Collins, van Duyse), coloboma of the choroid and iris (Seggel), polycoria (Rumschewitsch), bridge coloboma of the iris (Sæmisch, Talko), atypical iris coloboma (Plange), lamellar cataract (Berger), central cataract (Cohn, Horner), opaque nerve-fibres (Schleicher, Stephenson), microphthalmia (Michaelsen), congenital crescents (Stephenson).

Anatomical examination has been rendered possible by the cases demanding operative interference (v. supra), and has also been carried out on a post-mortem specimen by Wedl and Bock. The membranes contained very thin blood-vessels, almost invariably free from blood. The plaque consists of dense connective tissue with oval and spindle-shaped nuclei, covered by an incomplete endothelial membrane ; round and spindle-shaped cells may contain pigment. The filaments also consist of dense connective tissue, with flat long spindle or star-shaped cells, leucocytes and pigment. They pass directly into the iris stroma, from which they differ in no respect. The essential difference therefore between the persistent and the normal pupillary membrane consists in the extraordinary density of the connective tissue in the former and in its abnormal pigmentation (E. v. Hippel).

v. Michel gives a somewhat complicated explanation of the persistence of the pupillary membrane. He says that at the sixth fœtal month a peripheral fold is always formed in the iris, the concavity being directed forwards. Here the endothelial surfaces of the pupillary membrane fuse. As the anterior chamber grows traction is exerted, so that the membrane becomes thinned and atrophied in the centre, and a pupil is formed. In persistent pupillary membrane the separation of the fused surfaces does not occur, and holes form in the parts lying centrally owing to traction and countertraction.

The abnormal density of the membrane is the probable cause of persistence, though the cause of the density is a mere matter of conjecture. There is little evidence of inflammatory processes : the posterior synechiæ and pigment deposits are not necessarily inflammatory, since the former may be due to non-separation, and pigment in the stroma of the uveal tract is mostly formed after birth. Moreover the pigment here is probably hæmatogenous (cf. supra, Mayerhausen).

The cases of *anterior synechia of the persistent pupillary membrane and iris* demand separate consideration. They have been reported by Beck, Samelsohn, Makrocki, Zirm, Vossius, Wintersteiner, Silcock, Treacher Collins, Wüstefeld, Schapringer, van Duyse, Rumschewitsch, E. v. Hippel, and Ballantyne. There is no doubt that they were true pupillary membranes since they sprang from the lesser circle, and there were often remnants in the other eye. Cases have been examined microscopically by Wintersteiner, Collins, E. v. Hippel, and Ballantyne.

The usual two explanations have been advanced : (1) incomplete cleavage of the mesoblast which gives rise to the cornea and the pupillary membrane (Makrocki, Vossius, Treacher Collins, Wüstefeld, Rumschewitsch); (2) inflammation, with or without perforation, of the cornea (Beck, Samelsohn, Zirm, E. v. Hippel, van Duyse,
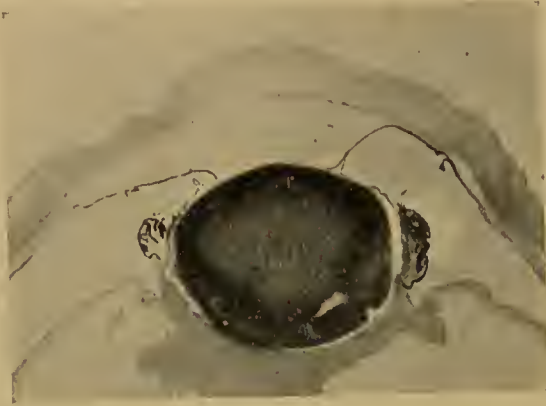
FIG. 560.—CONGENITAL ANTERIOR SYNECHIA.
Ballantyne, T. O. S., xxv. Anterior synechiæ of iris and persistent pupillary membrane. In the section only the iris synechia is seen; the pupillary membrane is seen passing forwards.

Wintersteiner). E. v. Hippel considers that both explanations may be true.

The inflammatory theory, taken in conjunction with the cases of congenital anterior staphyloma and adherent leucoma, seems the more

FIG. 561.—CONGENITAL ANTERIOR SYNECHIA.
Treacher Collins, Researches. Congenital anterior synechia of persistent pupillary membrane and iris.

probable, and is indeed proved in Wintersteiner's second case. In three cases there was blennorrhœa neonatorum, and in nearly all the others there was an opacity of the cornea at the site of union. Even in one of Treacher Collins's cases, where it is expressly stated that the cornea was clear, the microscopic examination revealed that " Bowman's membrane in the region of the anterior synechia is replaced by fibrous

tissue and Descemet's membrane is thickened." Whilst opacity of the cornea in the deeper layers might be reasonably explained on the developmental theory, it is difficult to believe that this would account for destruction of Bowman's membrane. The clearing up of the substantia propria is not surprising after inflammation at this early period, for the young cornea shows a marked tendency to clear. Moreover, the iris is quite well developed in these cases, though the pupillary edge may be adherent to the cornea (Vossius, Treacher Collins). The opacity at the back of the cornea may be pigmented, and such opacities occur associated with persistent pupillary membranes without anterior synechia (van Duyse); here the synechia has doubtless broken down. Krukenberg attributes cases of symmetrical pigmented plaques on the back of the cornea to remnants of the pupillary membrane. E. v. Hippel attributes congenital anterior synechia in one case to prolonged flattening of the cornea, whereby it is brought in contact with the iris.

JEANNULATOS.—Thèse de Paris, 1896. v. MICHEL.—A. f. O., xxvii, 2, 1881. RUMS-CHEWITSCH.—A. f. A., xx, 1889. ADOLF WEBER.—A. f. O., viii, 1861. MAYERHAUSEN.—Z. f. vergleich. Augenhkde., ii, 1883; K. M. f. A., xxiv, 1886. KEYSER.—Med. and Surg. Reporter, Philadelphia, 1880. KORN.—K. M. f. A., v, 1867. STEPHENSON.—T. O. S., xiii, 1893. SCHLEICH.—Wiener med. Presse, 1886. *FRANKE.—A. f. O., xxx, 4, 1884. SCHUBERT.—B. d. o. G., 1892. COHN.—C. f. A., v. 1881. v. HASNER.—Prager med. Woch., 1883. *WICHERKIEWICZ.—A. f. O., xxxiv, 4, 1888. *VAN DUYSE.—A. d'O., xxii, 1902; Encyclopédie franç., ii, 1905 (Bibliography). BERGER.—K. M. f. A., xxii, 1884. SEGGEL.—K. M. f. A., xxviii, 1890. BECK.—v. Ammon's Zeitschrift, i, 1831. SAMELSOHN.—C. f. A., iv, 1880. MAKROCKI.—A. f. A., xiv, 1885. ZIRM.—K. M. f. A., xxviii, 1890. VOSSIUS.—B. z. A., ix, 1893. WINTERSTEINER.—Wiener klin. Woch., 1893; A. f. O., lvii, i, 1903. SILCOCK.—T. O. S., xv, 1895. W. J. COLLINS.—R. L. O. H. Rep., xi, 1887; xii, 1888. TREACHER COLLINS.—T. O. S., xiii, 1893; Researches, London, 1896; in Norris and Oliver, System, 1897. WÜSTEFELD.—Z. f. A., iv, 1900. GRIMSDALE.—T. O. S., xxiii, 1903. *BALLANTYNE.—T. O. S., xxv, 1905. KRUKENBERG.—K. M. f. A., xxvii, 1899. E. v. HIPPEL.—In G.-S , 1900; A. f. O., lii, 3, 1901; lx, 3, 1905. JAMES.—T. O. S., xxi, 1901. SCHAPRINGER.—New Yorker Med. Monatschr., xii.

Corectopia.—The normal pupil is not situated exactly in the centre of the iris; it is usually slightly down and in, more rarely directly in, or in and up. In Patagonians it is said to be normally up and in (Kotelman). Gescheidt applied the name " corectopia " to considerable deviations from the normal. In well-marked cases the pupil is separated from the corneal margin by only one or two millimetres of iris. The greater the deflection, the greater usually is the *dyscoria* or distortion of the pupil.

The recorded cases of corectopia have been admirably collated and grouped by Best. He distinguishes four groups :

(1) Corectopia without other anomaly. This condition is not very uncommon : the direction of the ectopia is inconstant. The pupil is usually elongated and oval, triangular, or irregular, the sphincter is intact, and the reactions are normal. The condition is generally unilateral. The iris is normal, and shows no signs of inflammation : slight atrophic or aplasic changes may be observed—*e. g.* absence of the circulus minor.

(2) Corectopia with evidence of inflammation. The iris is discoloured, atrophic, irregularly pigmented : the pupil reacts badly or not at all : the radial fibres converge towards the atrophic part. The shape of the pupil shows all transitions to an iris coloboma. Sometimes a

corneal cicatrix points to perforation (Rindfleisch). The lens is normal in situation and transparency. Secondary glaucoma may occur (Samelsohn). These cases are probably due to intra-uterine inflammation.

(3) Corectopia with ectopia of the lens. This is the most common type. The cases have been collated well by Damianos. The pupil and lens are both displaced, and the iris is tremulous, especially in the area where the lens is absent. The condition is not hereditary, though the parents often show errors of refraction, especially myopia and astigmatism. Consanguinity has been noted by Pufahl and Best: the latter found several children affected in the same family, and in three families all the children—two to four in number—were affected. The condition is almost invariably bilateral, and in 72 per cent. of cases (31 out of 43) it is symmetrical: the ectopia may be in opposite directions in the two eyes. In thirteen cases the pupil was very small, even pin-point (*microcoria*); inequality of the pupils (*anisocoria*) is rare. Unilateral cases have been recorded by Wilde, Steffan, and van Duyse.

Damianos collected 44 cases—*i. e.* 88 eyes affected. The deviations were as follows: up and out, 35·2 per cent.; down and out, 13·6 per cent.; up and in, 13·6 per cent.; down and in, 7·9 per cent.; down, 11·3 per cent.; up, 9·1 per cent.; out 5·7 per cent.; in, 3·4 per cent.

The shape of the pupil may be round, oval, pear-shaped, triangular, slit-like (Brixa), or irregular. The iris is often normal in structure and reaction. Damianos found 16 abnormal: defective development of the sphincter or lesser circle, unequal development of the radial or circular fibres. The reaction is sometimes sluggish, sometimes absent, but here other complications—amaurosis, detached retina, glaucoma—were present.

The lens is usually clear; cataractous, with increase in size, ten times in 46 cases; diminished in size, four times (Samelsohn, Auerbach, Best, van Duyse). Lenticonus has been observed by Lindner. Out of 54 cases the lens was displaced in the opposite direction to the corectopia in 64 per cent. (Breitbarth): it was displaced laterally or in an intermediate direction in 24 per cent., and in the same direction as the pupil in 11·3 per cent. Coloboma of the lens may be seen, but the zonular fibres are generally intact. Remnants of the pupillary membrane were noted in 16·3 per cent. of cases. Coloboma of the choroid, etc., has not been observed, though temporal or circumpapillary depigmentation is not uncommon.

The refraction, as long as the lens is in the pupillary area, is myopic, sometimes with increased length of the eye—posterior staphyloma in 24 eyes out of 41 patients. The vision depends upon the situation of the lens, the fundus being usually normal: it is generally very defective.

(4) Corectopia, with other anomalies of the eye. The chief are: buphthalmia (v. Ammon, Mooren, Gillet de Grandmont, Kessler, Best); microphthalmia (v. Ammon); albinism (v. Ammon); epibulbar dermoid (v. Ammon); dermo-fibroma (van Duyse); coloboma of the lid (Talko, van Duyse). Corectopia is often nearly allied to iris coloboma, especially in the typical cases, where the distortion may be explained by traction of the sphincter in the coloboma.

Corectopia has been examined anatomically only by v. Ammon— inadequately—and by E. v. Hippel. The latter examined two cases and found that the narrow nasal part of the iris was three times the thickness of the drawn-out temporal part. There was no evidence of defective or increased development, and the condition was due to similar mechanical conditions to those found in an adherent iris. There was no perforation.

As to the cause of corectopia, Samelsohn assumes that the lens normally invaginates the optic vesicle in a direction from up and out to down and in ; hence the usual deviation of the pupil down and in. In corectopia there is excentric invagination. Best considers that the asymmetry should rather be of the optic cup, since Samelsohn's explanation would rather tend to homonymous ectopia of the iris and lens. Both hypotheses are purely conjectural. Best prefers to attribute the condition to defective development of the zonule, but it is expressly stated in many cases that the zonule is normal. Antonelli appeals to defective union of the layers destined to form the iris. There is no doubt that localised fœtal inflammation will explain many of the cases, and is probably the most satisfactory theory (cf. E. v. Hippel). van Duyse considers that pressure of the amnion is the cause, not only of corectopia, but also of polycoria, atypical colobomata of the iris, and luxations and opacities of the lens. The pressure is supposed to act both mechanically on the developing tissues, but also by interfering with the blood-supply, etc.

Kotelman.—Berliner klin. Woch., 1879. *Best.—A. f. O., xl, 4, 1894 (Bibliography). Rindfleisch.—B. d. o. G., 1892. Samelsohn.—Centralbl. f. d. med Wiss., 1875 ; Berliner klin. Woch., 1875. Pufahl.—C. f. A., iii, 1879. Wilde.—Malformations of the Organs of Sight, London, 1862. van Duyse.—A. d'O., xv, 1895 ; Encyclopédie franç., ii, 1895. *Damianos.—B. z. A., xxix, 1897 (Bibliography). Brixa.—K. M. f. A., xxxvi, 1898. Lindner.—Wiener med. Woch., 1895. Breitbarth.—Dissertation, Giessen, 1878. v. Ammon.—Klin. Darstellungen, iii, Berlin, 1841. E. v. Hippel.—A. f. O., li, 1, 1900 ; in G.-S., 1900. Antonelli.—Ann. di Ott., xxii, 1893. Pollak.—A. f. A., xxii, 1891. Holmes Spicer, Beaumont.—T. O. S., xiii, 1893. Fergus.—T. O. S., xiv, 1894.

Polycoria.—This is the condition in which there are holes in the iris.

They are not true pupils since they have no sphincter. The name should be restricted to actual holes in the iris, and should not include division of the pupil by bands of persistent pupillary membrane, bridge colobomata, etc. Diplocoria, or two pupils, is the commonest condition, though there may be eleven (Rumschewitsch), or even 16 (E. v. Hippel). Two equal pupils have not been seen in man, but v. Ammon records a case in a bull.

Franke distinguishes two groups : (1) rounded or slit-shaped holes near the pupillary edge (fourteen cases out of twenty-two) ; (2) holes at the ciliary border, resembling iridodialyses or colobomata (Talko, Mittendorf, Schelske). Mittendorf observed the second condition in a father and daughter. One had a central oval pupil and four triangular holes at the periphery, with the apices inwards. The other had a large opening at the periphery divided by a thin vertical band. In Talko's case there were numerous posterior synechiæ. Vossius, Franke, and Hilbert saw cases of a single con-

genital iridodialysis: v. Ammon's case, with two ciliary holes, he called iridodiastasis congenita.

The false pupils, having no sphincter, do not react to light, but vary in shape passively under the pupillary movements.

The condition is found associated with minute anterior synechiæ (Treacher Collins), typical coloboma of the iris in the other eye (Schapringer), corneal opacities, congenital cataract, and coloboma of the choroid.

As to the first group Manz considers them due to defective development of the mesoblast, Rumschewitsch to defective fusion of the mesoblastic layer with the optic vesicle. The second group may be due to intra-uterine or intra-partum traumatism, or to intra-uterine inflammation (fœtal iritis, Talko). In some cases of diplocoria (e. g.
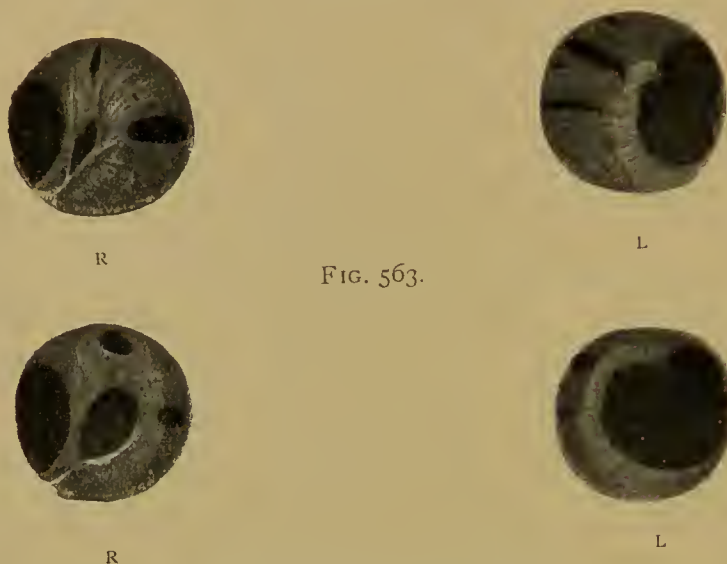
FIG. 562.

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FIG. 563.

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FIGS. 562 AND 563.—POLYCORIA.
Work Dodd, T. O. S., xiv. Fig. 562, undilated. Fig. 563, under atropin.

Wingenroth) it is difficult to eliminate persistence of the pupillary membrane. v. Ammon had recourse to proliferations at the pupillary border (corestenoma congenitum).

RUMSCHEWITSCH.—Medicyna, 1881; Rev. gén. d'O., iii, 1884; Westnik Ophth., 1887 E. v. HIPPEL.—In G.-S. 1900.   v. AMMON.—Klin. Darstellungen, 1841.   FRANKE — K. M. f. A., xxvii, 1889 (Bibliography).   MITTENDORF.—T. Am. O. S., 1884.   SCHELSKE.— Lehrbuch, 1874.   VOSSIUS.—K. M. f. A., xxi, 1883.   *HILBERT.—C. f. A., xxiv, 1900. TREACHER COLLINS.—T. O. S., xv, 1895; in Norris and Oliver, System, i, 1897.   SCHAP- RINGER.—New York Med. Jl., 1897.   MANZ.—Trans. International Congress, 1888. WINGENROTH.—C. f. A., xxiii, 1899.   WORK DODD.—T. O. S., xiv, 1894.   MAYNARD.— Indian Med. Gaz., 1897.

Aniridia, irideremia.—In this condition the iris is absent or extremely rudimentary. The condition may be regarded as a total coloboma of the iris, incomplete aniridia being indistinguishable from a large coloboma. It is almost invariably bilateral, unilateral irideremia having been reported only by Brunhuber (with buphthalmia) and Tokkus. The influence of heredity is seen in this abnormality more

than in any other ocular malformation. Thus Gutbier found 10 cases in four generations; Galezowski 31 cases in three generations; de Beck 7 aniridia and 2 colobomata in three generations; Mohr a mother with complete aniridia and two sons with partial.

Cases of incomplete aniridia have been recorded by Burnett, Vossius, Czapodi, Picqué, Fage, Tokkus, Franke, Claiborne, Strzeminsky, Griffith, but anatomical examination shows the condition is really always incomplete.

The appearance is characteristic: large black pupil occupying the whole area of the cornea, though usually somewhat less black than normal; red reflex when facing the light; photophobia, with consequent blepharospasm; often nystagmus and strabismus.

Coincident anomalies are the rule, affecting especially the cornea and lens. The cornea may show alteration in form—oval in the vertical meridian (Manz), conical curvature (Manz, de Benedetti)—opacities —arcus juvenilis (van Duyse, Laurentiew, Tokkus, Mohr)—microcornea (Felser), symmetrical small depressions in the inner quadrants near the limbus (Rindfleisch).

FIG. 564.—ANIRIDIA.

Treacher Collins, T. O. S., xiii. Anterior part of eye with apparent aniridia. The cornea and sclerotic have been removed, exposing a rudimentary iris, tags of pupillary membrane, lens with an anterior capsular opacity, and fibres of the suspensory ligament.

The anterior chamber is often abnormally deep, but this may be more apparent than real; it is very rarely shallow or absent (Ruete 3 cases, Schröter).

In the lens the commonest changes are anterior and posterior polar cataract (Nicolini, Felser, Pflüger, Goldzieher, Grossman); occasionally lamellar, or nuclear (Laurentiew). Partial cataract may clear up spontaneously, or per contra arise under observation. Luxation of the lens is not uncommon (Hjort, Jany, Klein, Samelsohn, Gouvea, J. v. Becker, Goldzieher); it is usually upwards. Hirschberg proved the possibility of both opacity and luxation developing in the course of years. Partial or complete absence

FIG. 565.—ANIRIDIA.

From the same case. A persistent tag of pupillary membrane is attached to the tip of the rudimentary iris, and there is a peripheral anterior synechia.

of the suspensory ligament has been recorded, but unless thickened it may easily escape observation; it is undoubtedly present in some cases. The ciliary processes were well developed in cases examined by Rindfleisch and Lembeck; in many cases they cannot be seen clinically. Since the aqueous is normal it would seem to follow that their function

is satisfactorily carried on. The same remark applies to accommodation and the ciliary muscle.

Other congenital abnormalities are persistence of tags of pupillary membrane, persistence of the hyaloid artery, ptosis, microphthalmia, buphthalmia (Brunhuber, Cabannès). Opacities in the vitreous, spots of choroidal atrophy, and detachment of the retina have been seen several times. The eyes have a considerable tendency to develop glaucoma (*e.g.* Brailey, Treacher Collins, de Schweinitz) : in one of Treacher Collins's cases this was simple, but in many cases there is ectopia of the lens, which is probably the cause of a secondary glaucoma. As will be seen from the anatomical arrangements, the conditions of lymph flow and filtration in these eyes are difficult (*see* " Glaucoma ").

Aniridia has been examined microscopically by Radius, Pagenstecher, de Benedetti, Lembeck, Rindfleisch, Treacher Collins, Hopf, A. H. Pagenstecher, and Bergmeister. In none of these cases, with the possible exception of one recorded by Hopf, was the iris completely absent. There was always a narrow rim of varying width ; this was either fused to the back of the cornea, or free in the anterior chamber (Rindfleisch). The sphincter is usually absent or extremely rudimentary ; there is often ectropion of the uveal pigment. There may be deposits of pigment around Schlemm's canal (Pagenstecher, Lembeck) or on the back of the cornea (Rindfleisch). The ciliary processes may be rudimentary (de Benedetti). The lens is sometimes small. Even when the iris is adherent to the cornea there are usually parts in which the ligamentum pectinatum is fairly well developed and free ; these account for the normal exit of intra-ocular lymph.

Various theories have been advanced to account for aniridia. Arnold thought that the absence of anterior ciliary vessels accounted for the non-development of the iris, but these are the vessels which supply the anterior vascular sheath of the lens. Sichel regarded the condition as a congenital mydriasis. Manz considered that the lens remained abnormally long in contact with the cornea, so that the growth inwards of the iris was mechanically impossible. The corneal opacities, anterior capsular cataracts, defects of the zonula, occasional absence of anterior chamber, etc., afford apparent support to this theory. It was supported by Goldzieher, Lembeck, and Treacher Collins. The great objection to the theory is the late period at which the iris develops, and E. v. Hippel adds that such an adhesion would prevent the proper formation of the substantia propria of the cornea. Rindfleisch considered that intra-uterine inflammation led to perforation at the limbus, loss of aqueous, and adhesion of the lens to the cornea. Such a bilateral peripheral perforation is in the highest degree improbable, and the investigation of his preparations by Leber and E. v. Hippel lend no support to the conjecture. It is obvious that any cause leading to arrest of development of the iris at any one point will account for an iris coloboma, and that the same cause acting simultaneously around the whole circle will account for aniridia. The coexistence of aniridia in one eye and adherent leucoma in the other (Vossius) lends some support to the idea of an inflammatory adhesion.

BRUNHUBER.—K. M. f. A., xv, 1877. *TORKUS.— Dissertation, Strasburg, 1888. GALEZOWSKI.—Rec. d'O., 1880. DE BECK.—T. Am. O. S., 1894. MOHR.—Dissertation, Jena, 1895. BURNETT.—A. f. A., iv, 1875. VOSSIUS.—K. M. f. A., xxi, 1883. CZAPODI.— FRANKE.—K. M. f. A, xxvii, 1889. PICQUÉ.—Anomalies de Développement, Paris, 1886. —T. O. S., xviii, 1898. CLAIBORNE.—New York Polyclinic, iii, 1894. GRIFFITH. FELSER.—K. M. f. A., xxvi, 1888. MANZ.—In G.-S., ii, 1876. DE BENEDETTI.—Ann. di Ott., xv, 1886. RUETE.—Lehrbuch, 1854. RINDFLEISCH.—A. f. O., xxxvii, 3, 1891; xxxviii, 1, 1892. K. M. f. A., xv, 1877. GOLDZIEHER.—C. f. A., xxi, 1897. KLEIN, SAMELSOHN.— BRAILEY.—T. O. S., x, 1890. HIRSCHBERG.—C. f. A., xii, 1888. CABANNÈS.—Ann. d'Oc., cxv, 1895. London, 1896. DE SCHWEINITZ —T. Am. O. S., 1891. TREACHER COLLINS.—Ophth. Rev., x, 1891; Researches, 1871. LEMBECK.—Dissertation, Halle, 1890. PAGENSTECHER.—K. M. f. A., ix, —T. O. S., xvi, 1896. BATTEN.—T. O. S., xx, 1900. HOPF.—Dissertation, Jena, 1900. STEPHENSON. JULER.—T. O. S., xxii, 1902. A. H. PAGENSTECHER.—A. f. O., lv, 1, 1902. *E. v. HIPPEL.—In G.-S., 1900. POTTER.—T. O. S., xxiii, 1903. BERGMEISTER.—A. f. O., lix, 1, 1904. *VAN DUYSE.— BLAIR AND Encyclopédie franç., ii, Paris, 1905 (Bibliography).

Anomalies of the pupillary margin.—So-called *ectropion of the uvea* occurs not only as an acquired condition (see Vol. I, p. 300) but also congenitally (Weinbaum), as is also shown in the anatomical examinations of aniridia (q. v.). The term is not a satisfactory one, but it has been still more erroneously applied to pigmented bodies at or near the pupillary margin, similar to those found in horses (v. Vol. I, p. 324). These are sometimes known as grape-clusters (Traubenkörner), flocculi. They may be enormously developed, but do not interfere with the movements of the iris. Occasionally they become free in the anterior chamber (Businelli, Fuchs, Troitzki, Bock, Apetz). In the horse they consist of aggregations of pigment epithelium on a basis of vascular connective tissue (v. Vol. I, p. 324). They probably have the same structure in these congenital deposits, and this accounts for the divergent observations recorded. Businelli and Troitzki found that they consisted of connective tissue with pigment and leucocytes. Bock found only pigment epithelium, and came to the extraordinary conclusion that they were remnants of pupillary membrane. In several cases minute cysts have been formed from the free masses.

Congenital *entropion of the uvea* has been described in one case by Enslin, the pigment epithelium being retracted backwards and outwards from the pupil. It can only be diagnosed microscopically, and it is doubtful if it is a congenital abnormality.

WICHERKIEWICZ.—A. f. O., xxvii, 1, 1891. WEINBAUM.—K. M. f. A., xxx, 1892. BUSINELLI.—Ann. d'Oc., lx, 1868. FUCHS.—A. f. A., xv, 1885. WEDL AND BOCK.—Atlas, 1886. TROITZKI.—A. f. A., xvii, 1887. BOCK.—K. M. f. A., xxvi, 1888. APETZ.—Z. f. A., iv, 1900. HARTRIDGE.—T. O. S., xxii, 1902. ENSLIN.—A. f. A., li, 1905.

Congenital Cysts.—*See* Vol. I, p. 318.
Nævus. Melanoma.—*See* Vol. I, p. 322.

THE LENS

Lamellar Cataract.—*See* Vol II, p. 401.
Central or Nuclear Cataract.—*See* Vol. II, p. 404. The near relationship of central cataract to lamellar has been already mentioned. In families with congenital cataract the lamellar type has often been found in one generation, central in another. Cases of unilateral central

cataract have been described by Schirmer (1891) and Oncken (1901). Hess has observed a combination of the two conditions in both eyes of the same patient. He lays stress upon the fact noticed by himself, Schirmer, and Oncken that the nucleus is often situated abnormally far back in the lens. Some light is thrown upon this anomaly by the condition found in a fowl embryo which Hess examined. Here the lens vesicle did not become separated from the corneal epiblast, so that the capsule was not closed and the corneal epithelium passed directly into lens epithelium. The lens fibres proliferated through an opening in the cornea, where they were destroyed and thrown off. It is probable that if the development had been allowed to continue the lens vesicle would have finally closed and become separated. The subsequent development of normal fibres would then have produced the picture of a congenital central cataract.

A similar mechanism may account for the disc-shaped congenital cataracts which have been described by Becker, Vossius, Treacher Collins, and Hess (v. Vol. II, fig. 291).

A central cataract which may be regarded as the ultimate expression of a lamellar cataract with very extensive nuclear changes is seen in some cases with dense central and punctate peripheral opacities. Anatomical examination shows that these are flattened lenses, spindle-shaped in section, with a very thin layer of clear cortical fibres (Hess).

SCHIRMER.—A. f. O., xxxvi, 4, 1890. ONCKEN.—Dissertation, Marburg, 1901. BECKER. —Zur Anat. d. gesunden u. kranken Linse, Wiesbaden, 1883. VOSSIUS.—B. z. A., ix, 1893. TREACHER COLLINS.—T. O. S., xviii, 1898. *HESS.—In G.-S., vi, 2, 1905.

Total Cataract.—*See* Vol. II, p. 404. General opacity of all the lens fibres at first—usually a uniform grey-white cataract—is somewhat rarer than nuclear cataract. Becker observed the transformation of a lamellar, at the age of eight weeks, into a total cataract at the age of eleven months, and anatomical investigation shows that the condition is, at any rate in some cases, fundamentally the same (Hess). The dependence of total cataract, as of lamellar, upon some constitutional condition is insisted upon by Becker. The microscopical features of one such case have already been described (v. Vol. II, p. 404).

Some total cataracts, showing a chalky white mass in the pupillary area, with deep anterior chamber and iridodonesis, are shrunken lenses, forming a link with the membranaceous cataracts. The latter are probably due to an intra-uterine inflammation (Vüllers, Lor) which may be of a syphilitic nature (Gunn, Colburn, Axenfeld).

BECKER.—Zur Anat. d. gesunden u. kranken Linse, Wiesbaden, 1883. HESS.—A. f. O., xlvii, 2, 1898; in G.-S., vi, 2, 1905. VÜLLERS.—A. f. O., xl, 3, 1894. LOR.—Soc. Belge d'O., 1897. AXENFELD.—Münchener med. Woch., 1904.

Spindle (v. Ammon), **fusiform** (Pilz), **axial** (Knies), or **coralliform** (Marcus Gunn) **Cataract.**—*See* Vol. II, p. 402. Fusiform cataract. which was first definitely described as congenital by Becker, may be either an axial filamentary opacity or consist of tube-like radii with ampulliform endings, giving a close resemblance to coral. Described first by v. Ammon (1833), later by Pilz (1850), E. Müller (1855), O. Becker (1876), their intimate relation to lamellar and central cataract

was brought forward by Knies (1877). This author attributed the peculiar shape to adhesion of the nucleus to the anterior and posterior capsule, whereby the nucleus is drawn out into a spindle by the further development of the cortex. Many cases of adhesion to the anterior capsule have been described, whereas union with the posterior capsule is not proved. Vossius (1893) accepted this explanation, and one of his cases is interesting in that a typical fusiform cataract in one eye was associated in the other with a lamellar cataract from the anterior surface of which a filament passed forwards to an anterior capsular cataract. The explanation of Knies finds further confirmation in the case of the fowl embryo described by Hess (v. p. 806). Bach's researches have already been considered

Fig. 566.—Coralliform Cataract.
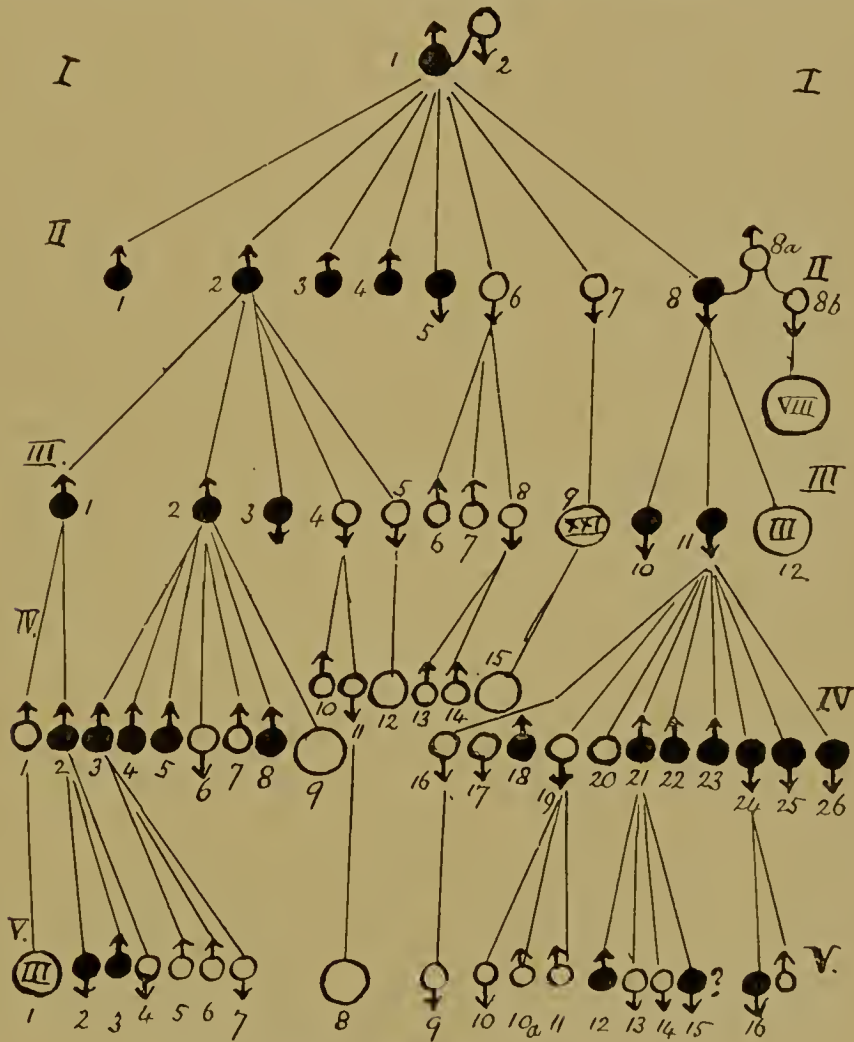Marcus Gunn, T. O. S., xv.

Fig. 567.—Heredity in Coralliform Cataract.

Nettleship, R. L. O. H. Rep., xvi. ♂. Male unaffected. ●. Male with cataract. ♀. Female unaffected. ♀. Female with cataract. O. Several children free from cataract. I, II, III, IV, V. Five generations.

(*v*. Vol. II, p. 402). The hereditary factor and the occurrence of the condition as a familial disease have been pointed out by several observers, a remarkable genealogy being given by Nettleship (Fig. 567).

v. AMMON.—Z. f. O., iii, 1833; Klin. Darstellungen, 1833. PILZ.—Prager Virteljahrs-schrift, xxiv, 1850. E. MÜLLER.—A. f. O., ii, 2, 1855. O. BECKER.—Zur Anat. d. gesunden u. kranken Linse, Wiesbaden, 1883. KNIES.—A. f. O., xxiii, 1, 1877. LEBER.—A. f. O., xxvi, 1, 1880. VOSSIUS.—B. z. A., ix, 1893. MARCUS GUNN.—T. O. S., xv, 1895. BACH.—A. f. O., xliii, 1, 1897; xlv, 1, 1898. FISHER.—T. O. S., xxv, 1905. NETTLESHIP.—R. L. O. H. Rep., xvi, 3, 1905.

Anterior capsular cataract.—*See* Vol. II, p. 407. That anterior capsular and cortical cataracts may be congenital is shown by a number of cases in which other forms of congenital cataract have been present simultaneously (*e. g.* Vol. II, fig. 291). Hulke first pointed out the possibility of anterior capsular cataract without perforation of the cornea in the young (*v*. Vol. II, p. 416). Becker considered that the condition was caused by intra-uterine inflammation, with or without perforation. Hess considers it more probable that some impediment to the separation of the lens vesicle retards the closure of the anterior capsule (*v*. p. 806). Cases with bilateral anterior capsular cataracts without any sign of inflammatory or other disturbance strongly support this view.

Posterior cortical cataract.—*See* Vol. II, pp. 417, 421. Some congenital posterior cortical cataracts are allied to the lamellar group, as is shown by their association with them either in the same or in the opposite eye. Some occur in association with posterior lenticonus (q. v.) or spurious posterior polar cataract. The latter, due to persistence of part of the posterior vascular sheath of the lens, are treated elsewhere, since they are not true cataracts. The frequency of acquired posterior cortical cataract as an expression of malnutrition (*v*. Vol. II, p. 421) makes it probable that some congenital cases may be due to intra-uterine inflammation.

Cataract in Microphthalmia.—The lens is often cataractous in microphthalmia (q. v.), and is not infrequently displaced (*v. infra*). All stages of retrogression of the fibres are met with, even to persistence only of the capsule and a few epithelial cells (*cf.* Wiegels). The remnants may be calcified.

WIEGELS.—A. f. O., l, 1900.

Lenticonus.—In lenticonus the anterior or posterior surface of the lens is spheroidal. Only two cases of anterior lenticonus have been described (Webster, van der Laan).

More than 20 cases of posterior lenticonus have been reported, and about half have been examined anatomically. F. Meyer (1888) first described the clinical features, and he was followed by Knapp, Eiseck, Mitvalsky, Gullstrand, Elschnig, Cramer, and others. There are often posterior cortical opacities (Meyer, Eiseck, Mitvalsky, Gullstrand, Elschnig), but the lens may be clear (Knapp, Cramer). In Mitvalsky's case there was also persistent hyaloid artery, a feature drawing attention to the congenital origin of the defect. L. Müller's case showed a central myopia of 13 D. and a peripheral of 4 D. Pergens

described a case with pyramidal cataract. Several cases have been observed in animals—three in rabbits by Bach, others in rabbits and pigs by Hess.

In about four fifths of all the cases there were opacities in the lens. Four clinical cases were undoubtedly congenital. In several cases there were other developmental anomalies, especially persistent hyaloid artery, a point of ætiological importance (Hess). Persistent hyaloid artery was present in two human cases, and in 60 per cent. of animal eyes examined microscopically.

Clinically the condition must be distinguished from false lenticonus (Demicheri), which is often found in old age, and is due to the increasing difference in refractive index of the nucleus as compared with the cortex.

In most of the cases observed anatomically there has been a rupture of the posterior capsule, the cortex projecting through the rent (Hess, Bach, Bäck, Denig, Pergens). The rupture is attributed by Bach to traction by the persistent hyaloid artery, and Hess agrees that the rupture is primary and caused in some manner by the persistent posterior vascular sheath. Pergens on the other hand considers that the rupture is produced by proliferation of the lens-fibres, a sort of new growth which he calls phakoma. Mulder examined rabbits whose parents had received tubercular inoculations into the anterior chamber ; his results confirm those of Hess. A similar picture is also occasionally produced by traumatic rupture of the posterior capsule in man (Treacher Collins). E. v. Hippel has also observed changes in rabbits' lenses which must be attributed to rupture of the capsule, probably due to intra-uterine inflammation. In two of three cases of persistent hyaloid artery which I have reported the posterior capsule of the lens was defective in the centre, and in the third the appearances were suggestive of a rent (v. infra). Persistence of the hyaloid artery cannot, however, be the only factor, since this abnormality may be absent. Displacement backwards of the nucleus is probably a constant feature, and is similar to that found in other congenital abnormalities, except that there is usually much distortion.

WEBSTER.—A. f. A., iv, 1874. VAN DER LAAN.—Period. de Oftalm., 1880. PLACIDO.— Period. de Oftalm., 1881. F. MEYER.—C. f. A., xi, 1888. DOYNE.—T. O. S., ix, 1889. KNAPP.—A. f. A., xxii, 1890. KNAGGS.—Lancet, 1891. WEEKS.—A. of O., xx, 1891. TREACHER COLLINS.—T. O. S., xi, 1891. EISECK.—K. M. f. A., xxx, 1892. GULLSTRAND. —Nord. ophth. Tidskr., v, 1892. MITVALSKY.—C. f. A., xv, 1892. HESS.—A. f. O., xxxix, 1, 1893; xlii, 3, 1896; Z. f. A., i, 1899; in G.-S., vi, 2, 1905. L. MÜLLER.—K. M. f. A., xxxii, 1894. ELSCHNIG.—K. M. f. A., xxxiii, 1895. LANG.—T. O. S., xv, 1895. SYM.— Ophth. Rev., xiv, 1895. CRAMER.—K. M. f. A., xxxiv, 1896. MULDER.—K. M. f. A., xxxv, 1897. BACH.—A. f. O., xlv, 1, 1898. BÄCK.—A. f. A., xxxiv, 1898. PERGENS.—A. f. A., xxxv, 1898; Z. f. A., vii, 1902. DENIG.—Ophth. Record, 1899. MARSHALL.—T. O. S., xxv, 1905.

Ectopia lentis.—Congenital malposition of the lens, or ectopia lentis, should be distinguished from traumatic dislocation, or luxatio lentis (Sippel, 1859). Ectopia lentis is almost invariably bilateral ; a unilateral case is described by Page. The edge of the lens is seen in the pupillary area, though it is usually necessary to dilate the pupil. The division of the aperture into a phakic and an aphakic part may
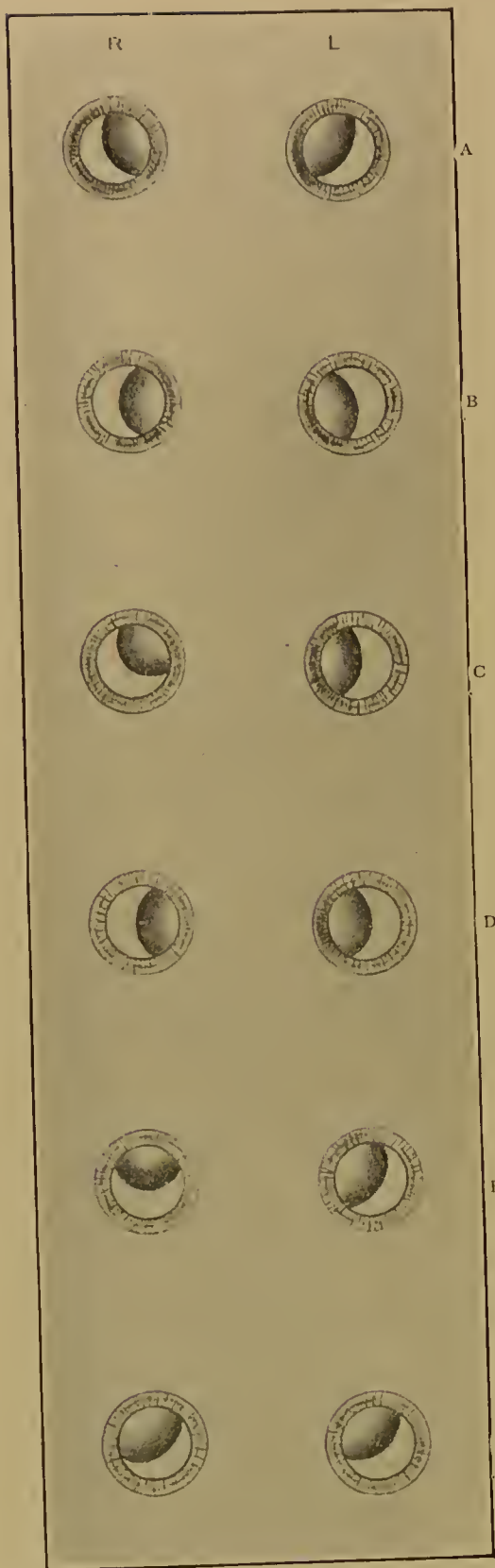
FIG. 568.—ECTOPIA LENTIS.
Morton, R. L. O. H. Rep., ix.   See text.

cause uniocular diplopia or binocular quadruplication (Heddæus, Knapp). The anterior chamber is deepened on the aphakic side. The edge of the lens appears by reflected light as a dark crescent, the outer border being very sharp, the inner shading off. This appearance is due to the strong prismatic refraction ; by altering the incidence of the light, as by transillumination through the sclera, the edge appears as a bright crescent. Though usually convex outwards, the edge of the lens may be nearly straight, and both forms may occasionally be found in coloboma lentis without ectopia.

In most cases, though not in all, the suspensory ligament is completely or almost completely absent in the aphakic area (v. Graefe). As a result of the failure of the zonula and the plasticity of the young lens the phakic area often has a high myopic refraction ; in a boy æt. 9 the refraction in the phakic area was — 15 D., in the aphakic + 10 D. (Hess). Slight degrees of ectopia occur, leading to lenticular myopia and astigmatism ; in many of these cases the cause could only be determined by accurate investigation of the Purkinje images.

The displacement of the lens is usually upwards and is symmetrical in the two eyes ; in 73 cases the direction in both eyes was upwards in 30, up and out in 18, up and in in 8, down in 5, inwards in 4, outwards in 3, down and out in 1 ; in 1 case the right was inwards, the left down and in ; in 3 cases the displacement was asymmetrical—twice right down and out, left down and in, once right down and in, left up and in (Dorsch). Damianos found the displacement usually up and in. Rogman has described a case of double ectopia downwards, with coloboma of the lens (cf. Marcus Gunn). Displace-
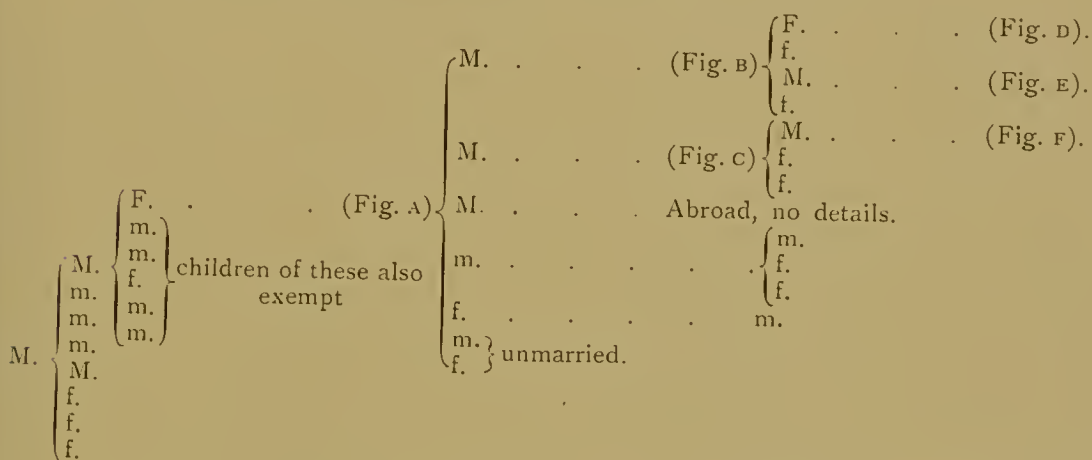
ment backwards has been recorded (Becker). As already mentioned, Page has reported a case of unilateral ectopia lentis.

The lens is generally clear—in 46 cases Damianos found it opaque six times on both sides, four times on one only; the condition differs in this respect from traumatic luxation. It is usually stated that the lens is smaller than normal, and this is probably true in most cases; it depends, however, upon the observation of the frequency of spontaneous dislocation into the anterior chamber, and this may be explained by the softness of the juvenile lens (Hess). Lindner reports four cases in which the lens was larger than normal in all its diameters.

In most cases of ectopia lentis there is also a coloboma of the iris, usually in the opposite direction: corectopia (Jones), irideremia, nystagmus, etc., have been observed.

The hereditary factor is very pronounced in some of the recorded cases (v. Graefe, Dixon, Williams, Frickhöfer, Sattler, and others). Morton records a family history in which ectopia lentis occurred presumably in five successive generations comprising ten individuals, and certainly in three successive generations comprising seven individuals (fig. 568).

The genealogy of the undoubted cases is as follows:

```
                                                              ⎧F.  .    .  (Fig. D).
                                                              ⎪f.
                                       ⎧M. .   .  (Fig. B)⎨M. .    .  (Fig. E).
                                       ⎪                  ⎪t.
                                       ⎪                  ⎩
                                       ⎪                   ⎧M. .   .  (Fig. F).
                                       ⎪M. .   .  (Fig. C)⎨f.
                                       ⎪                  ⎩f.
           ⎧F. .      .  (Fig. A)⎨M. .   .   Abroad, no details.
           ⎪m.                       ⎪                   ⎧m.
      ⎧M.⎨m.⎫                        ⎪m. .   .    .   .  ⎨f.
      ⎪   ⎪f.⎬children of these also ⎪                   ⎩f.
      ⎪m.⎪m.⎪     exempt             ⎪f. .   .   .   .  m.
      ⎪m.⎩m.⎭                        ⎪m.⎫
M.⎨m.                                ⎩f.⎬unmarried.
  ⎪M.
  ⎪f.
  ⎪f.
  ⎩f.
```

Lewis found sixteen cases in six generations of one family.

Ectopia lentis has been examined anatomically only in two cases complicated by traumatism and in cases of microphthalmia or other widespread anomalous development. The condition has been attributed to fluidity of the vitreous, failure of the suspensory ligament, etc. (v. Graefe, Quaglino). The frequency of displacement upwards suggests some relationship to the closure of the secondary optic vesicle, and this view is supported by observations on cases in which the hyaloid artery persists and the vitreous undergoes atypical development (Hess, Treacher Collins) (v. infra). In the latter condition fibrous bands are formed in the lower part of the vitreous in relation with the fœtal cleft; these not only displace the lens upwards, but may also pull it backwards. They are formed very early in fœtal life, so that it is not improbable that they may entirely disappear before birth, the displacement of the lens alone remaining (Hess). Samelsohn's con-

jecture, that the lens invaginates the primary optic vesicle at an abnormal situation, is not supported by these observations, and would probably lead to much more extensive anomalies.

v. Graefe.—A. f. O., i, 1, 1854; ii, 1, 1855. Stellwag v. Carion.—Wiener med. Wochenbl., 1856. Dixon.—R. L. O. H. Rep., i, 1857. Sippel.—Die spontane Luxation der Linse, etc., Marburg, 1859. Jeaffreson.—R. L. O. H. Rep., vii, 1871. Page.—Lancet, 1874. Jones.—Dublin Jl. of Med. Sc., 1879. Morton.—R. L. O. H. Rep., ix, 1879. D'Oench.—A. f. A., ix, 1880. Power.—Lancet, 1881. Mules.—Ophth. Rev., ii, 1883. Fryer.—Amer. Jl. of Ophth., 1884. Cross.—T. O. S., v, 1885. de Benedetti.—Ann. di

FIG. 569.   FIG. 570.

FIGS. 569 AND 570.—ECTOPIA LENTIS, ETC.
Marcus Gunn, T. O. S., ix. Fig. 569 shows pupil undilated; Fig. 570, pupil dilated. Note the change in appearance of the pigmented margin, also the ectopia and coloboma of the lens, and the suspensory ligament.

Ott., xv, 1886. Thompson.—Ophth. Rev., vi, 1887. Heddaeus.—K. M. f. A., xxvi, 1888. Marcus Gunn.—T. O. S., ix, 1889. Holmes Spicer.—T. O. S., x, 1890. Griffith.— T. O. S., xvii, 1897. Stephenson, Keeling, Batten.—T. O. S., xx, 1900. Dorsch.— Dissertation, Marburg, 1900. Lewis.—A. of O., xxxiii, 1904. Damianos. B. z. A., xxix, 1897.

The Retina and Optic Nerve.

Aplasia of the retina and optic nerve.—The retina and optic nerve are aplasic in anencephaly (Manz, v. Wahl, Mayou, and others), in cyclopia (q. v.) (van Duyse), in some cases of hydrocephalus (Rosenbaum), etc. The nerve-fibres are entirely absent, as well as the ganglion-cells; the outer layers of the retina may be quite normal. In micro-phthalmia (q. v.) and anophthalmia (q. v.) the optic nerve may be absent. Absence of the optic nerve in the presence of a more or less well-developed eye predicates the proper formation of the primary optic vesicle.

Brière described a case of a girl æt. 17 with congenital absence of the discs, though the central vessels were seen. This ophthalmoscopic observation has been confirmed anatomically in the rabbit by Bach and Rosenbaum, who found the papilla replaced by a depression in the sclerotic, filled with retinal nuclear layer cells; from this a cone of connective tissue passed forwards towards the lens and ciliary region.

Various explanations have been adduced for aplasia of the retina and optic nerve. It has been regarded as secondary to the very extensive cerebral disease which is usually present: anencephaly

itself has been attributed to hydrocephalus followed by rupture (Förster, Ahlfeld), to pressure of the amnion (Dareste, Marchand,

FIG. 571.—DEVELOPMENT OF OPTIC NERVE.
Mayou, T. O. S., xxiv. Coronal section of human embryo, 1 cm. long, showing early differentiation of mesoblast to form optic nerve sheath before formation of axis cylinders in the nerve.

FIG. 572.—DEVELOPMENT OF OPTIC NERVE.
Mayou, T. O. S., xxiv. Coronal section of human embryo, 2·5 cm. long, showing optic nerve sheath differentiated and connected with dura mater; traces of axis cylinders can be seen under higher power.

Duval, Perls), and over-curvature of the embryonic axis, whereby closure of the medullary canal is prevented (Lebedeff). More

FIG. 573.—DEVELOPMENT OF OPTIC NERVE.
Mayou, T. O. S., xxiv.   Another section from the same embryo.

FIG. 574.—ANENCEPHALY.
Mayou, T. O. S., xxiv.   Lateral view, showing deficient frontal eminences
and proptosis.

recently it has been suggested (Petrén) that the condition of the retina and optic nerve is the result of a " system defect "—*i. e.* to a defect in the neurones of a particular order.[1] In the retina the neurones of the first order, *i. e.* the rod and cone bipolars, are usually intact, only those of the second order, *i. e.* the ganglion-cells, being absent ; their axons, the optic nerve fibres are then necessarily also absent.

This theory is ingenious, but the facts can be equally well explained on the theory of a secondary degeneration, such as occurs in post-natal life. There is not sufficient evidence to justify dogmatism as to the true ætiology.

FIG. 575.—ANENCEPHALY.
From the same specimen. Posterior view of head, showing open spinal canal.

Mayou's observations on a case of anencephaly are held by him to support the view that the optic nerve fibres have a cerebral origin or are at least dependent upon the integrity of the cerebral centres : the latter conjecture is certainly the more probable. Mayou points out that the nerve-sheath is normally developed before any axis cylinders are present in the nerve (figs. 571–3). His case of anencephaly showed arrest of development at this stage (figs. 574–581). The optic nerves showed complete absence of axis cylinders ; the disc was deeply cupped, owing partly to absence of nerve-fibres, partly to weakness of the lamina cribrosa which yielded to the intra-ocular

[1] *See* PARSONS, ' The Neurology of Vision,' London, 1904.

FIG. 576.—ANENCEPHALY.

From the same specimen. Front view of macerated skull, showing the shallow orbits and wide spheno-maxillary fissures.

FIG. 577.—ANENCEPHALY.

From the same specimen. View of skull from above, showing absence of vault, deficient foramen magnum, large semicircular canals, and openings of the optic foramen.

pressure. In the retina the outer layers were fairly normal, pigment epithelium, rods and cones, and nuclear layers being present. Ganglion-
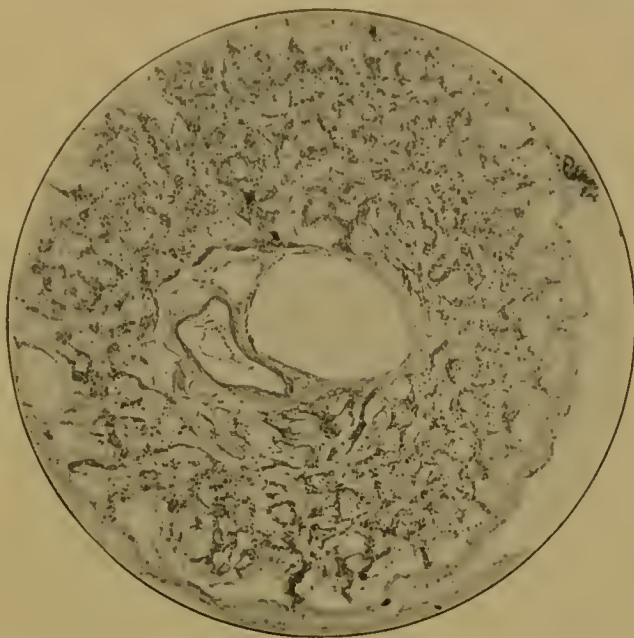

FIG. 578.—ANENCEPHALY.
From the same specimen. Transverse section of optic nerve, showing empty trabeculæ. Note the large central artery and vein.

FIG. 579.—ANENCEPHALY.
From the same specimen. Longitudinal section of optic nerve, showing absence of axis cylinders.

cells were present, though they were not so numerous and their staining reactions were not so good as in the normal eye. The nerve-

fibre layer was absent, as shown by the vessels lying in contact with the hyaloid membrane.

These highly pathological conditions are not suited, from their

FIG. 580.—ANENCEPHALY.

From the same specimen. Horizontal section through the posterior part of the eye, showing deep cupping of the disc.

FIG. 581.—ANENCEPHALY.

From the same specimen. Retina and choroid, showing dilated vessels and absence of nerve-fibre layer.

very nature, to decide difficult physiological problems. They should be permitted to afford only corroborative, or at least non-discordant,

evidence. It is obvious that serious pathological processes, occurring at a very early stage of fœtal life, may be followed by degenerative changes which are most elusive.

Manz.—Virchow's Archiv, li. v. Wahl.—Dissertation, Dorpat, 1839. Mayou.— T. O. S., xxiv, 1904. Rosenbaum.—Dissertation, Marburg, 1902. Brière.—Ann. d'Oc., lxxviii, 1877. Förster.—Die Missbildungen des Menschen, Jena, 1861. Ahlfeld.—Die Missbildungen des Menschen, Leipzig, 1880. Dareste.—Sur la Production artificielle des Monstruosités, Paris, 1877. Perls.—Lehrbuch d allgem. Path., Stuttgart, 1894. Lebedeff.
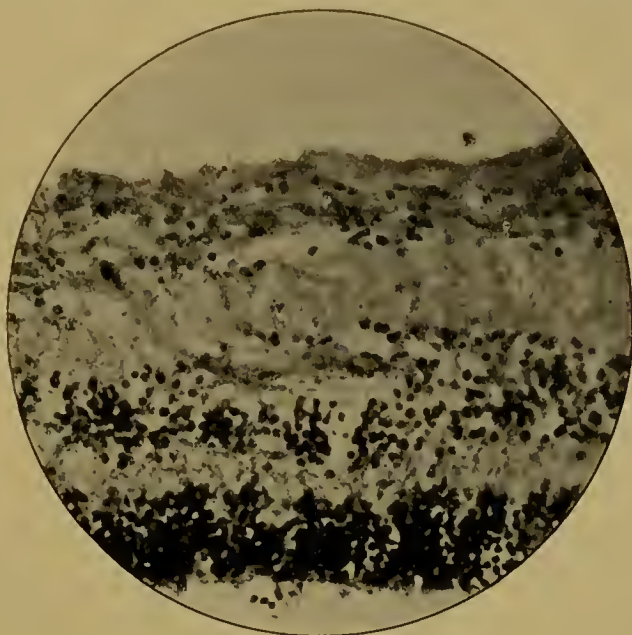

FIG. 582.—ANENCEPHALY.
From the same specimen. Retina, showing ganglion-cell layer above.

—Virchow's Archiv, xxvi, 1881. Petrén.—Virchow's Archiv, cli, 1898. Dötsch.— A. f. O., xlviii, 1, 1899. *van Duyse.—A. d'O., xix, 1899; Encyclopédie franç., ii, Paris, 1905.

Medullated nerve=fibres in the retina.—*See* Vol. II, pp. 545, 656.

Anomalies of the optic disc.—Various minor anomalies of the disc have been described from time to time. They require little more than passing mention here. Most have been described from the ophthalmoscopic appearances, and have not been examined anatomically: a considerable number of ophthalmoscopic examples have been collected by Szili.

The disc may be *inverted* (Fuchs), the vessels emerging from the nasal instead of the temporal side; they regain the normal disposition beyond the disc. The disc is often malformed—irregular in outline, square or polygonal—especially in cases with inferior crescent: the eyes are often hypermetropic, and correction fails to elicit normal vision. When the condition is more extreme the disc may be incompletely formed, as in cases shown by Magnus and Szili: in the former all the vessels emerge from the temporal edge, and the edges show excess of pigment; in the latter the disc is semilunar. Eversbusch

describes a triangular, excavated disc associated with opaque nerve-fibres.

(For other anomalies of the disc *see* " Persistent Hyaloid Artery ").

PURTSCHER.—A. f. A., xii, 1883. MAGNUS.—K. M. f. A., xxii, :884. EVERSBUSCH.—K. M. f. A., xxiii, 1885. SZILI.—Augenspiegelstudien, Wiesbaden, 1901.

COLOBOMATA OF THE EYE

The term "coloboma," introduced by P. v. Walther (1821), is used to indicate certain congenital defects of characteristic appearance and situation. Typical colobomata are associated, in situation at any rate, with the fœtal (so-called choroidal) fissure, through which the mesoblast invaginates the posterior part of the eye. Similar congenital defects are, however, not infrequently observed in situations which cannot be explained by any relationship with the fœtal cleft; these are called atypical colobomata.

It will be remembered that the fœtal cleft is formed at a very early stage, almost simultaneously with the formation of the secondary optic vesicle and the invagination of the lens—*i. e.* during the first month. It is a ventral invagination which extends back for a short distance into the optic pedicle, thus allowing the entry of the central retinal vessels. The cleft soon becomes closed, but the line of closure remains for a time apparent from the fact that when pigment begins to be deposited in the retinal pigment epithelium it remains unpigmented; this is the case until the sixth week in man. It was formerly held by some observers that the eye underwent a rotation subsequently, so that the fœtal cleft, from being ventral or ventral and slightly mesial, became lateral, the fovea centralis being developed in it (Huschke, v. Baer, Krause). This theory has been completely abandoned, the *coup de grace* having been given by Chievitz.

v. WALTHER.—v. Graefe and v. Walther's Jl., ii, 1821. CHIEVITZ.—Internat. Monat-schrift f. Anat. und Phys., iv, 1887; Anat. Anzeiger, ii, 1888; iii, 1889; Arch. f. mikr. Anat., 1889; Arch. f. Anat. und Phys., 1890.

Coloboma of the iris, iridoschisma (Gescheidt).—Bartholinus (1673) first described and figured a coloboma of the iris; the next obser-vation was by Albinus (1764); the early bibliography will be found in Himly's book. Gescheidt (1831), Heyfelder (1834), and others demon-strated the heredity of coloboma of the iris: Rosas (1829) found it in three sisters and in two or three generations. Bloch (1774) met with central cataract concomitantly in several members of the same family.

Typical coloboma of the iris is the usual condition, the pupil being continued into a cleft downwards or down and slightly in. The hiatus varies in size, generally from one sixth to one fifth or even one quarter of the total surface. The usual form is a gothic arch, with the apex downwards, so that the peripheral part is narrower than the pupillary. Colobomata are often partial, not reaching the ciliary border. The edges may not converge, but be parallel or diverge downwards; the coloboma may be so extensive in the last case as to merit the designa-tion " partial aniridia " (q. v.). Partial coloboma may be a mere indenta-

tion of the pupillary margin. The normal projection of the pigment epithelium slightly beyond the pupillary edge of the stroma is usually somewhat emphasised in the limbs of the coloboma, and may form nodules, festoons, or filaments. The pigment layer may fill the coloboma or its apex, the stroma only being defective. More rarely there is a bridge of pigment, but such bridges—*bridge coloboma*—are generally composed of persistent strands of pupillary membrane projecting from the lesser circle. The bridge may be attached to the actual edge of coloboma, there being no evidence of pupillary membrane (Hilbert).

The relief of the iris varies much, dependent chiefly upon the condition of the sphincter. This is continued around partial colobomata, but usually fades off along the edges of complete ones. The behaviour of the coloboma in pupil reaction and under

Fig. 583.—Coloboma of the Iris.
After Lawson.

atropin or eserin varies. The pupil is often displaced downwards, very rarely upwards.

Typical coloboma of the iris is one of the commonest abnormalities of the eye. It is usually unilateral, and on the left side (3 : 2—Bock). There is generally a coloboma of the choroid, but by no means invariably.

In most partial colobomata the hiatus is continued downwards as a pigmented streak or a furrow; the pigment is distinguished from a melanoma in being situated beneath the surface of the iris. *Pseudo-coloboma* (Cornaz) is a narrow pale radial streak in the usual situation, showing defective development of pigment. Many slight modifications in pigmentation and in the relief of the iris point to a tendency to the formation of a coloboma, and may be met with in conjunction with colobomata of deeper parts (Bock).

Atypical colobomata of the iris differ only in their direction : they have been called pseudo-colobomata by v. Mittelsdorf and Rumschewitsch : this term was applied by Manz to incomplete atypical colobomata. The statistics of Bock, Rumschewitsch, and v. Hippel show the relative frequency of different directions thus : Out, in, up and out, up and in, up, down and out, in the proportions 12 : 9 : 7 : 6 : 5 : 3 (van Duyse).

The literature is as follows :

Fig. 584.—Bridge Coloboma of the Iris.
Treacher Collins, T.O.S., xxvi.

Outwards : Mittelstädt (1880), Bayer (1881), Makrocki (1884), Franke (1885), Nuel and Leplat (1889), Lang (1890), Plange (1890), Rumschewitsch (1891), Frost (1893), Raehlmann (1897), Leber, van Duyse.

Inwards : Heyl (1887), Mittelstädt (1880), Makrocki (1884), Czapodi (1885), Steinheim (1886), Rindfleisch (1892), Seggel (1893), Bock (1893), McGillivray (1898).

Up and out : Hutchinson (1870), Theobald (1888), Page (1890), Bock (1893), Pfannmüller (1894), McGillivray (1898), Leber.

Up and in : v. Reuss (1886), Schiess-Gemuseus (1887), Fage (1890), Pollak (1890), Hess (1892), Leber.

Upwards : Theobald (1888), Rumschewitsch (1891), Simonson (1892), Bock (1893), McGillivray (1898).

Down and out : E. v. Hippel (1898), Lechner (1900), Leber. These only represent the more recent cases : of historical interest are those of Acrell (1773) and Helling, upwards ; Warnatz, up and out ; Helling, Heyfelder (1834), inwards ; Conradi, Seiler, Dressel, outwards.

Atypical colobomata may involve a quarter or half of the iris, thus, like the typical, merging into aniridia, and the other eye may show aniridia (Rindfleisch, Czapodi) (q.v.). The shape is as in the typical— egg-shaped, gothic arch, pear-shaped, bridge coloboma (Quaglino, Seggel, van Duyse). The sphincter may extend round the ciliary border (Wagenmann), or far down the limbs (McGillivray). Remnants of persistent pupillary membrane are probably not quite so common as in typical colobomata (Plange, Rumschewitsch). Atypical colobomata may be total or partial, and the partial ones often show a pigmented line (Lechner) or a raphe (Mittelstädt), as in the typical. Similarly there may be a deficiency of pigment, retinal (Franke) or of the stroma, or there may be heterochromia (van Duyse). The persistent rim in partial coloboma may show other signs of imperfect development or atrophy.
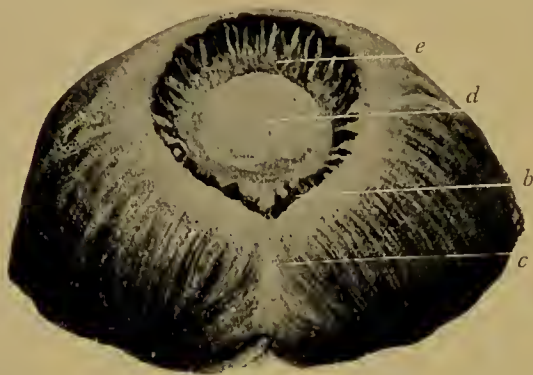

FIG. 585.—COLOBOMA OF IRIS, CILIARY BODY, AND CHOROID.

Marshall, R. L. O. H. Rep., xv. The cornea, sclerotic, and iris have been removed. *e.* Ciliary body. *d.* Lens. *b.* Coloboma of ciliary body. *c.* Raphe in ciliary body.

In typical coloboma it is usual to find coincident coloboma of the choroid, noted by v. Ammon, and often of the ciliary body (Gescheidt) and lens. Other malformations are persistent pupillary membrane, variations in size, form, or curvature of the cornea, opacities in the lens, strabismus, nystagmus, coloboma of the optic nerve, coloboma of the lid and hare-lip (Heyfelder), epibulbar dermoid, microphthalmia (Schön, v. Walther, v. Esscher, v. Ammon, Gescheidt), and rarer abnormalities in the head, trunk, or limbs.

In atypical cases colobomata of deeper parts of the eye are the exception, though they have been found (Steinheim, Nuel and Leplat, Frost, Hess (lens)). Mittelstädt, v. Reuss, and Hess observed typical downward coloboma of the choroid associated with atypical coloboma of the iris. Cataract (Hess), palpebral coloboma, and epibulbar dermoid (Schiess-Gemuseus) have been seen.

Colobomata of the iris may be *multiple* : these are confused in the literature with polycoria and varieties of persistent pupillary membrane (Stellwag, Rumschewitsch, Bock). Bock described a triple partial coloboma in a pig, the pupil being triangular, with the apex down—*i. c.* a combination of a typical with two atypical colobomata. Other cases

are—down, and up and out, in a fowl (v. Ammon); in, and out, two cases (v. Ammon); in, and out (Lerche); down, and in (Tortual); down, and in (Emers, Magnus); down, and out (Manz).

Coloboma of the iris has been examined microscopically, most exhaustively by Bock. The edges are of normal thickness in the upper part, but much thickened and nodular in the lower. As observed clinically, the retinal pigment epithelium is over-developed at the margins, often projecting beyond them. The sphincter may be absent, or may spread out and be lost. Abnormally profuse development of vessels may be seen in the lower part, as well as nodular aggregations of round cells. Sections of a raphe in partial coloboma show triangular depression of the surface, with projection or depression of the posterior surface.

Bridges are formed of connective tissue differing from the iris stroma; they may arise from the lesser circle (persistent pupillary membrane), from the edges of the coloboma, or from the projecting masses of pigment.

In some cases a fibrous strand stretches from the papilla or its vicinity forwards around the equator of the lens to be attached to the apex of the coloboma.

Care must be taken to avoid diagnosing as colobomata cases of extreme retraction of the iris, due to fœtal or infantile inflammation (cf. E. v. Hippel).

Himly.—Die Krankheiten u. Missbildungen des menschl. Auges, Berlin, 1843. Gescheidt.—Dissertatio de Colobomate iridis, Lipsiæ, 1831. Hilbert.—Virchow's Archiv, 1891. *Bock.—Die angeborenen Colobome des Augapfels, Wien, 1893. *Rumschewitsch. —A. f. O., xxxvii, 1, 1891. *E. v. Hippel.—A. f. O., xlvii, 1, 1898; in G.-S., 1900. *van Duyse.—Encyclopédie franç., ii, Paris, 1905. Mittelstädt.—A. f. A., ix, 1880. Makrocki.—A. f. A., xiv, 1884. Franke.—C. f. A., viii, 1885. Nuel and Leplat.— Ann. d'Oc., ci, 1889. Lang.—T. O. S., x, 1890. Plange.—A. f. A., xxi, 1890. Frost.— T. O. S., xiii, 1893. Raehlmann.—Bibl. med., 1897. Leber.—In G.-S. (E. v. Hippel), 1900. Heyl.—Ann. d'Oc., lxxvii, 1877. Czapodi.—In Nagel's Jahresbericht, 1885. Steinheim.—C. f. A., ix, 1886. Rindfleisch.—A. f. O., xxxviii, 1, 1892. Seggel.— K. M. f. A., xxxi, 1893. McGillivray.—Ophth. Rev., xvii, 1898. Schiess-Gemuseus.— K. M. f. A., xxv, 1887. Pollak.—A. f. A., xxii, 1890. Hess.—K. M. f. A., xxx, 1892. Theobald.—Amer. Jl. of Ophth., 1888. Simonson.—Dissertation, Berlin, 1892. Griffith. —T. O. S., xviii, 1898. Lechner.—K. M. f. A., xxxviii, 1900. E. v. Hippel.—A. f. O., lii, 3, 1901. de Vries.—A. f. O., lvii, 3, 1904. Treacher Collins.—T. O. S., xxvi, 1906.

Coloboma of the ciliary body.—Erdmann (1826), from the absence of visible ciliary processes in a coloboma of the iris, conjectured the presence of a coloboma of the ciliary body: this cannot be considered any proof. Anatomically the ciliary body has been repeatedly shown to take part in the abnormality which affects the choroid and iris: it has also been observed as an isolated phenomenon. It is invariably in the typical position—downwards (v. infra, however, Hess), but it must be remembered that atypical coloboma of the iris and choroid have not been submitted to microscopical investigation. As already stated, coloboma of the ciliary body is normal in Cochin China fowls (Lieberkühn).

The condition shows much variation in size and arrangement. There is usually a pigmented or unpigmented stripe extending from the ciliary processes into the choroid. When more developed the ring of

ciliary processes is broken by an anterior indentation and a corresponding posterior rounded projection : the processes abutting this indentation are deflected obliquely and pushed somewhat backwards. These neighbouring processes vary greatly in size ; they may be diminutive, or much enlarged, especially on the temporal side, covering the actual defect, though there may be no definite cleft. The retinal epithelium may show enormous hyperplasia, affecting particularly the unpigmented inner layer, so that large yellowish polypoid masses may project into the vitreous.

The floor of the coloboma is covered with vascular connective tissue, which eventually becomes spongy. It may be raised into a crest, containing islets of cilio-retinal epithelium. The pigmented epithelium usually stops at the margin. The ciliary muscle may be absent, or cleft, being replaced by loose vascular connective tissue.

Hess has described a rudimentary coloboma of the ciliary body inwards in a case with nasal coloboma of the lens. The ciliary processes were thickened, retracted, and irregular. Bock twice observed complete absence of the ciliary body on the temporal and nasal sides associated with extensive colobomata.

ERDMANN.—Zeitschrift f. Natur- u. Heilkunde, iv, 1826. LIEBERKÜHN.—Arch. f. Anat. u. Phys., 1879. NUEL AND LEPLAT.—Ann. d'Oc., ci, 1889. *BOCK.—Die angeb. Colobome des Augapfels, Wien, 1893. HESS.—A. f. O., xlii, 3, 1896. VAN DUYSE.—Encyclopédie franç., ii, Paris, 1905.

Coloboma of the choroid and retina.—This condition was first observed by v. Ammon (1831), and drawn by Ruete. It is most commonly associated with coloboma of the iris, but 20 or 30 cases have been recorded in which the iris was quite normal (Hoffmann, v. Becker, Horstman, Eichhoff, Talko, van Duyse). The terms " typical " and " atypical " are used for this deformity in the same sense as for coloboma of the iris—i. e. the typical form is downwards or down and slightly in. The condition is usually bilateral (2 : 1), and more marked in the left eye ; when unilateral, the left eye is most often affected (Panas).

On examination with the ophthalmoscopic mirror alone a very bright reflex is seen from the part affected, the pigment being almost or completely absent. The coloboma is usually oval or comet-shaped, with the rounded end at or near the disc. The anterior end may or may not be visible ophthalmoscopically. The coloboma may even include the disc, which is generally transversely oval. There is often a depression on the lower part of the disc even when it is not included in the coloboma. Greater transverse than vertical diameter is rare (7 mm. by 3 mm., Litten). The edges are usually pigmented, either continuously or partially : the pigment may invade the coloboma to a greater or less degree, giving a tigroid appearance. Tongues or islets of normal fundus may invade the area (e. g. Hirschberg).

The level of the coloboma is almost invariably below that of the rest of the fundus, as shown by parallax in the vessels : it often varies in depth, having localised ectasiæ. In many cases the coloboma is divided into two lateral ectatic halves by a median ridge.

There are two types of vessels in the colobomata, retinal and ciliary.

The former are easily recognised by their continuity with the other retinal vessels: they may be limited to the marginal part or course over the whole defect. The ciliary vessels, derived from the short posterior ciliary, are more tortuous and broader, resembling choroidal vessels, and lying beneath the retinal. They can often be seen as they emerge from the sclerotic, suddenly appearing in the floor of the coloboma and spreading out and branching. The inferior vortex vein is usually absent in typical colobomata and the lateral ones are displaced outwards. The retinal vessels often pass upwards as they emerge from the disc, and other anomalies occur when the coloboma involves the disc (*see* " Coloboma of the Optic Nerve ").

Large colobomata extending around the disc must often involve the position of the macula, and in other cases the characteristic appearances of the macula are frequently absent: it may be quite normal (Saemisch, Cohn). Anatomically a normal fovea has not been met with. On the other hand, the vision may be quite good, though it is generally very defective, owing to anomalies in shape and curvature of the cornea, coloboma or opacities of the lens, high myopia, choroido-retinitis, optic atrophy, etc. Apparent complete absence of both choroids except at the maculæ has been recorded by Tatham Thompson (*cf.* also Landman).

The cornea is often characteristic in its shape—that of an egg, with the pointed end downwards—as well as its smallness (micro-cornea), the combination leading to marked astigmatism. Considerable, and often excessive, myopia is the rule, due to relative increased length of the eye. The field of vision generally shows a defect corresponding with the coloboma, but rarely so extensive. Schmidt-Rimpler proved that even in these cases there is generally light perception in the defective area, and Haab showed perception of red and blue. Benson demonstrated constriction of the field at the periphery, without any scotoma. Photophobia, strabismus, and nystagmus are not infrequently present.

Besides coloboma of the iris and ciliary body, persistent pupillary membrane has been noted (Schiess-Gemuseus, Seggel), also nuclear cataract (Ebhart), anomalies of the cranium, deaf mutism, hare-lip, etc. Evidences of choroido-retinal inflammation are the rule, and progressive cataract is common: these eyes are frequently the seat of nutritive and chronic inflammatory trouble.

Atypical coloboma of the choroid and retina is very rare. The following cases have been collected by van Duyse:

(1) With coloboma of the iris—Steinheim (1886), right anophthalmia, left internal coloboma of the iris, internal coloboma of the choroid including the disc; Nuel and Leplat (1889), left external coloboma of the iris, indication of coloboma of the disc, external coloboma of the choroid three disc-diameters from the papilla; Frost (1893), external coloboma of the iris and of the choroid.

(2) Without coloboma of the iris—Pflüger (1884), bilateral external colobomata of the choroid involving the discs, with choroido-retinal lesions; Nuel (1885), right external coloboma from disc to macula; Lang (1886), coloboma up and out, with buphthalmia; Randall and de Schweinitz (1889), left internal coloboma with translucent, greenish,

falciform prolongation into the vitreous, ending in filaments; Lindsay Johnson (1890), coloboma of the optic nerve, discontinuous infero-external coloboma of the choroid ("extra-papillary coloboma"); Pfannmüller (1894), coloboma external to the macula; Rindfleisch (1894), ectatic extra-papillary coloboma upwards; E. v. Hippel (1901), bilateral coloboma up and out, with unilateral interstitial keratitis and anterior synechia.

(3) Atypical coloboma of the iris, with typical coloboma of the choroid—Mittelstädt (1880), left internal iris coloboma, infero-internal choroidal coloboma including the disc; v. Reuss (1891), left supero-internal iris coloboma, infero-internal choroidal coloboma reaching disc, infero-internal conus; Hess (1892), bilateral supero-internal colobomata of the irides, colobomatous and cataractous lenses, right typical choroidal coloboma including disc; [Bock (1893), bilateral supero-internal colobomata of irides, inferior conus in each disc; Lechner (1900), right infero-internal coloboma, inferior conus.]   (The last two cases do not strictly belong here.)

Of the nine cases recorded in the first two groups the colobomata were directed upwards in five, inwards in two, down and out in one, and upwards in one.   The vision was nearly normal (Randall and de Schweinitz, Pfannmüller), mediocre (Nuel and Leplat, Rindfleisch), or much diminished (Pflüger, Steinheim).   The field of vision could not be determined in Pflüger's and Steinheim's cases, and is not recorded in those of Noel and Leplat, Frost, and Rindfleisch.   In Randall and de Schweinitz' case the blind spot was enlarged, with retention of light perception.   Pfannmüller found no defect.   Atypical colobomata of the choroid have not been examined microscopically.

Typical colobomata of the choroid have been frequently examined microscopically, but the interpretation of the results is by no means easy.   The condition of the individual coats of the eye in the area affected undoubtedly varies much in different cases.   The so-called choroidal cleft is the line of fusion of the lips of the secondary optic vesicle; hence the condition of the two layers is of prime importance. A priori it was conjectured that these must be absent over the coloboma: this, far from being the fact, is the exception, though the layers are often so attenuated and malformed as to be scarcely recognisable.   The pigment epithelium, or outer layer, is usually lacking for the most part in large colobomata, but minute examination shows that non-pigmented islets occur, and the whole area is occasionally covered entirely with retinal epithelium devoid of pigment.   Usually the pigment epithelium fades off from the periphery towards the centre, the cells becoming more and more free from pigment (partial leucosis, Pause), smaller, rounded, and finally unrecognisable.   Leber and Hess have pointed out that a non-pigmented tissue may arise from the epithelium which is wholly unrecognisable as such without exhaustive investigation.

Total absence of the inner layer, or retina proper, is equally un-common: reduced to its minimum, the membrana limitans interna is seen binding the edges of the coloboma together (E. v. Hippel).   More rarely, but beyond dispute, retina, more or less altered but quite recognisable, covers the whole surface (Haab, Pause, Mannhardt, Bach): in

the cases of Pause and Bach it was apparently normal. E. v. Hippel rightly points out that absence at the exact line of suture could only be asseverated from frontal sections, and in most cases the eyes are cut meridianally. All varieties of defective structure are seen in the retina —irregularity of the layers, especially deflection of the nuclear layers, rosette-like structures (*v.* Vol. II, p. 632), internally displaced rods and cones, cystic spaces, fusion with the sclera or specific adventitious tissue.

Doubling of the retina has been observed in several cases, the edges being turned outwards (Haab, Becker, van Duyse), or inwards (Deutschmann). In the ciliary coloboma of Cochin China fowls, which is a normal phenomenon, the edges of the retina are regularly turned outwards (Lieberkühn).

The choroid is usually absent over the coloboma, but may be present, more or less well developed; according to Pause it was quite normal in one case—a condition which scarcely corresponds with a coloboma at all from the clinical standpoint. The lamina fusca is probably generally normal (*e. g.* Talko), except possibly in the bluish types of coloboma. The chorio-capillaris is absent; Hirschberg found an atrophic, non-pigmented choroid; da Gama Pinto traced it into the coloboma, where it gradually faded off; Deutschmann and Bock found the choroid inflamed. Generally the choroid stops at the edge, where it is thickened, and shows aggregations of round cells and pigment cells. The retina, choroid, and sclera are often fused together at the margin of the coloboma.

The commonest condition of the floor of the coloboma is probably that in which there is a thin fibrous membrane (Haase, 1870) which shows few or no traces of retina or choroid (" intercalary " membrane). The origin of this membrane can only be matter for conjecture.

The sclerotic is much thinned in the ectatic cases, though there is a localised thickening in the situation of a median raphe (Thalberg). In less ectatic cases the sclera thins off gradually, mostly by loss of the inner layers. This also occurs in the anterior and posterior parts of ectatic colobomata, whilst the lateral margins usually show normal or increased thickness, the edges projecting over the ectasia. The ectasiæ may much resemble the ordinary myopic posterior staphyloma. The more ectatic the coloboma the more are the congenital cysts associated with microphthalmia simulated (q.v.).

A median raphe may be bifid at the posterior part (Bock): or it may be limited to the anterior part. It often contains blood-vessels, and the edges of the secondary optic vesicle may be demonstrable at the edges (Hess), sometimes as a toothed or comb-like structure (Bock). Peculiar vascular strands of connective tissue may stretch forwards to the back of the lens, ciliary body, etc. (Eversbusch, da Gama Pinto, Tartuferi, Hänel, Hess, Bach). These are probably persistent hyaloid artery and aplasic vitreous (Hess) (*see* " Microphthalmia ").

Evidences of more or less recent inflammation in these eyes, especially in the uveal tract, are not uncommon (Deutschmann, Höltzke, Thalberg, van Duyse, Bock, Wood). There can be little doubt that they are peculiarly vulnerable, and no great stress must be

laid upon these observations from the point of view of an inflammatory pathogenesis. Hence the importance of examining cases early in life (Bach, van Duyse).

v. BECKER.—A. f. O., xxii, 3, 1876. HORSTMANN.—Charité Annalen, 1877. TALKO.—K. M. f. A., xxviii, 1891; xxix, 1892. LITTEN.—Virchow's Archiv, lxvii, 1876. HIRSCHBERG.—C. f. A., viii, 1885. SAEMISCH.—K. M. f. A., v, 1867; A. f. O., xv, 3, 1869. COHN.—In Nagel's Jahresbericht, 1871. TATHAM THOMPSON.—T. O. S., xix, 1899. LANDMAN.—A. f. A, liv, 1906. SCHMIDT-RIMPLER.—A. f. O., xxiii, 4, 1877; xxvi, 2, 1880. BENSON.—Dublin Med. Jl., 1882. SEGGEL.—K. M. f. A., xxviii, 1890. EBHART.—Ann. di Ott., xviii, 1889. STEINHEIM.—C. f. A., ix, 1886. NUEL AND LEPLAT.—Ann d'Oc., ci, 1889. FROST.—T. O. S., xiii, 1893. PFLÜGER.—A. f. A., xiv, 1884. NUEL.—Ann. d'Oc., xciii, 1885. LANG.—T. O. S., vi, 1886. RANDALL AND DE SCHWEINITZ.—A. f. A., xix, 1889. LINDSAY JOHNSON.—A. f. A., xxi, 1890. PFANNMÜLLER.—Dissertation, Giessen, 1894. RINDFLEISCH.—K. M. f. A., xxxii, 1894. MITTELSTÄDT.—A. f. A., ix, 1880. v. REUSS.—In Rumschewitsch, A. f. O., xxvii, 4, 1891. HESS.—K. M. f. A., xxx, 1892. *BOCK.—Die angeb. Colobome des Augapfels, Wien, 1893. LECHNER.—K. M. f. A., xxxviii, 1900. PAUSE.—A. f. O., xxiv, 1, 1878. LEBER.—Ueber die Ursachen u. Entstehung der Entzündung, Leipzig, 1891. HESS.—A. f. O., xlii, 3, 1896. HAAB.—A. f. O., xxiv, 2, 1878. MANNHARDT.—A. f. O., xliii, 1, 1897; Mittheil a. d. Hamburger Staatskrankenanstalt, 1899. *BACH.—A. f. O., xlv, 1, 1898. BECKER.—A. f. O., xxxiv, 1888. DEUTSCHMANN.—K. M. f. A., xix, 1881. LIEBERKÜHN.—Arch. f. Anat. u. Phys., 1879. HIRSCHBERG.—C. f. A., v, 1881. DA GAMA PINTO.—A. f. A., xiii, 1883. HAASE.—A. f. O., xvi, 1, 1870. THALBERG.—A. f. A., xiii, 1884. EVERSBUSCH.—B. d. o. G., 1883. TARTUFERI.—In Nagel's Jahresbericht, 1884. HÄNEL.—Dissertation, Erlangen, 1886. WOOD.—T. O. S., xii, 1892. HESS.—A. f. O., xxxiv, 3, 1888; xxxvi, 1, 1890. HÖLTZKE.—A. f. A., xii, 1883. *E. v. HIPPEL.—In G.-S., 1900; A. f. O., lii, 3, 1901. LEWINSOHN.—A. f. O., lvii, 2, 1903. *VAN DUYSE.—A. d'O., xvi, 1896; Encyclopédie franç., ii, Paris, 1905.

Macular coloboma (central coloboma).—The term "coloboma of the macula" should be used only in a topographical sense to indicate a partial atypical coloboma of the choroid and retina, since, as already mentioned, the macula is not developed in the foetal cleft (v. p. 820). Early cases were described by v. Ammon (1852), Streatfield, Talko, Reich, de Wecker; Bock (1893) collected 31 cases and added others; 10 or 15 more have been recorded since. Some of Lindsay Johnson's extra-papillary colobomata and other similar cases are either macular or paramacular.

Otherwise resembling ordinary colobomata, macular coloboma is distinguished by its shape—usually horizontally oval, more rarely round (Kimpel) or angular (van Duyse). The transverse diameter varies from 1 to 10 papilla diameters, the vertical from 1 to 3 P.D.; about 3 P.D. in the horizontal is the average. There is generally some ectasia—1–6 D (maximum 10 D, Bock), varying in different parts. The edges are usually sharp, with a line of pigment, and often a yellowish zone outside: the surface may be covered with patches of black pigment.

As in other colobomata, there are both retinal and ciliary vessels. Both sets are usually small. Large branches of posterior ciliary vessels were seen emerging from the floor in Kimpel's case, and the ciliary branches may form a convoluted network (Wiethe, Lindsay Johnson ("naevi"), as in a unique case reported by Beaumont. The retinal vessels may pierce the centre of the coloboma and disappear.

The condition was bilateral in the cases of de Wecker, Schmidt-Rimpler, Fuchs, Dor, Bock, Kastalsky, Kimpel. When unilateral the left eye is the more commonly affected. As regards refraction, in 20

cases 11 had moderate myopia, 5 high myopia, 6 hypermetropia, and 1 emmetropia (Bock). Myopia may be independent of ectasia of the coloboma (Schnabel, Kimpel, Bock). Vision is usually poor, but may be fair (Reich).

Defect in the field may be absent or impossible to determine. Absolute scotoma was noted by Schnabel, Michaelsen, Bock, the last with vision $= \frac{6}{6}$, which could only be consistent with a paracentral scotoma (E. v. Hippel). Kastalsky found a ring scotoma, with good central vision; relative scotoma is common, with colour perception diminishing towards the periphery (van Duyse), relative scotoma greater than the area of the coloboma with total scotoma over the nasal part (van Duyse).

Coincident other anomalies are comparatively rare. Ordinary posterior staphyloma has been noted by Streatfield, de Wecker, and Wiethe, and disseminated choroiditis frequently (Schnabel, Wiethe,

FIG. 586.—MACULAR COLOBOMA.
After Lawson.

Dor, Silex, Lindsay Johnson, Lister). Besides these, congenital anomalies are: persistent pupillary membrane (Michaelsen), aniridia (Montmeja, a doubtful case), coloboma of the optic nerve (Dor, Michaelsen, Lindsay Johnson), microphthalmia (Michaelsen), microphthalmia with coloboma of iris, choroid and optic nerve (Wood), microcephaly (Dor). In a remarkable case recorded by Silcock a persistent hyaloid artery was attached to the centre of the coloboma and extended forwards to the back of the lens, expanding there in the usual manner.

Macular coloboma has been examined microscopically by Bock, Hess (rabbit), Zimmermann (dog), Deyl, van Duyse. In Bock's case the choroid and pigment epithelium were absent, and the retina formed a very thin membrane with remnants of the nuclear layers. In Deyl's case the choroid resembled scleral tissue, with much pigment about the vessels; the retina covered the whole area, but the inner layers became thin and the outer disappeared at the edges. van Duyse's case

was a cyclopic eye, upon which little stress can be laid from the present point of view; the retina was rudimentary, and the choroid and pigment epithelium were absent. Hess found ectasia with thinning of the sclera to one tenth the normal, absence of choroid, reduction of the retina to a very delicate fibrous membrane. In Zimmermann's case the retina and choroid were absent.

v. Ammon.—Münchener med. Zeit., 1852. Streatfield.—R. L. O. H. Rep., v, 1866. Talko.—K. M. f. A., viii, 1870. Reich.—K. M. f. A., x, 1872. de Wecker.—K. M. f. A., x, 1872. *Bock.—Die angeb. Colobome des Augapfels, Wien, 1893. Lindsay Johnson.—A. f. A., xxi, 1890. Kimpel.—A. f. A., xxxvii, 1898. Wiethe.—A. f. A., xiv, 1884. Beaumont.—T. O. S., xi, 1891. Schmidt-Rimpler.—A. f. O., xxvi, 2, 1880. Fuchs.—A. f. O., xxviii, 1, 1882. Dor.—Rev. gén. d'O., 1887. Kastalsky.—A. f. A., xxxvi, 1897. Schnabel.—Wiener med. Blätter, 1884. Michaelsen.—C. f. A., xiii, 1889. Wood.—T. O. S., xii, 1892. Silex.—A. f. A., xviii, 1888. Lister, Silcock.—T. O. S., xx, 1900. Hess.—A. f. O., xxxvi, 1, 1890. Zimmermann.—K. M. f. A., xxxv, 1897. Deyl.—Internat. Congress, Moscow, 1897. *E. v. Hippel.—In G.-S., 1900. *van Duyse.—Ann. d'Oc., xci, 1884; xcvi, 1886; xcviii, 1887; A. d'O., xix, 1899; Encyclopédie franç., ii, Paris, 1905. Parsons and Coats.—Brain, xxix, 1906.

Coloboma at the optic disc (coloboma of the optic nerve, or of the optic nerve sheath).—Coloboma at the optic disc is rare (3 in 12,000
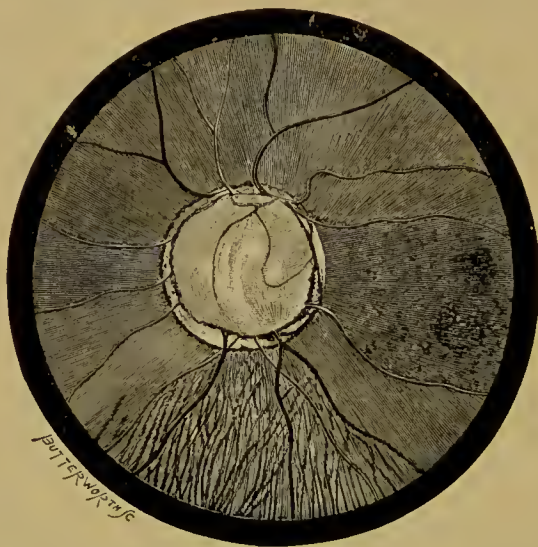

Fig. 587.—Coloboma of the Optic Nerve.
Parsons, T. O. S., xxi.

patients, Vossius): Caspar (1885) collected 20 cases, Saemisch (1891) brought the total up to 48. The appearances are very various; the most constant are increase in size and irregularity in shape of the pseudo-disc; partial or total ectasia of the surface, usually deepest in the lower part; whiteness of the surface, with grey patches at localised ectasiæ, due partly to shadows; special arrangement of the vessels.

The shape is generally round or vertically oval; the size may be from twice to twenty times the diameter of the disc. Total excavation is uncommon (e. g. Caspar, Blessig, van Duyse); greater depth of the lower part is the rule (Nieden); lateral ectasiæ have been described by Remak and Fehr. Secondary ectasiæ—little pockets separated by

projecting bands—occur with or without general ectasia (Schöler, Wiethe, Remak, Schnabel, Stood, Bock). The position of the optic nerve tissue, usually the upper part, is generally pink.

Caspar has divided the arrangement of vessels into three groups : (1) all the vessels emerge from the lower part of the pseudo-disc, even those which subsequently turn upwards ; (2) they emerge at or a little above the centre, and are nearly normally arranged ; (3) the vessels appear at the edges around the whole circumference.

Vision has been found to be normal several times, or it may be absent (Caspar, a case of retinitis pigmentosa) ; usually it is seriously defective. The field has been noticed diminished concentrically (van Duyse), and in the upper part (Nieden). Strabismus and nystagmus may be present.

FIG. 588.—PIGMENTED COLOBOMA OF THE OPTIC DISC.
Thomson and Ballantyne, T. O. S., xxiii.

Coloboma at the disc is often associated with coloboma of the choroid, which may or may not enclose the disc. Atypical colobomata are also met with—of the iris (Lechner), macula (Michaelsen, Lindsay Johnson), choroid (Lindsay Johnson). Other concomitant anomalies are persistent hyaloid artery (Becker, Bayer, Remak, v. Reuss, Makrocki, van Duyse, Hegg, Ginsberg, and others), remnants of posterior sheath of the lens (Pfannmüller), opaque nerve fibres (Eversbusch, Würdemann, Tereschkowitsch), choroido-retinitis (Eversbusch, Ginsberg), opacities in the lens, lenticonus, corectopia. Coloboma at the disc is met with in 20 per cent. of microphthalmic eyes (e.g. Blessig, Hegg, Lindsay Johnson, Pfannmüller, Weiss and Görlitz, Loktew, E. v. Hippel). The cornea was abnormally small in one case in an otherwise normal eye.

Anatomical investigation of coloboma at the optic disc has been carried out in 20 cases (3 in rabbits) (v. Ammon, Liebreich, Hess, van Duyse, Manz, Bock, Ginsberg, Bach, Görlitz, Elschnig, Parsons and Coats). The essential characteristic is the enormous enlargement of the foramen scleræ, in which the choroid and pigment epithelium are absent and are replaced by connective tissue. Retinal elements and nerve-fibres are present. In the walls are cystic spaces or the wall itself may be so ectatic as to form a large cyst (Bock, Görlitz, van Duyse), thus forming an intermediate stage in the production of microphthalmic cysts.

The condition of the central retinal vessels is of prime importance: in five of the cases they were not contained in the nerve itself, so
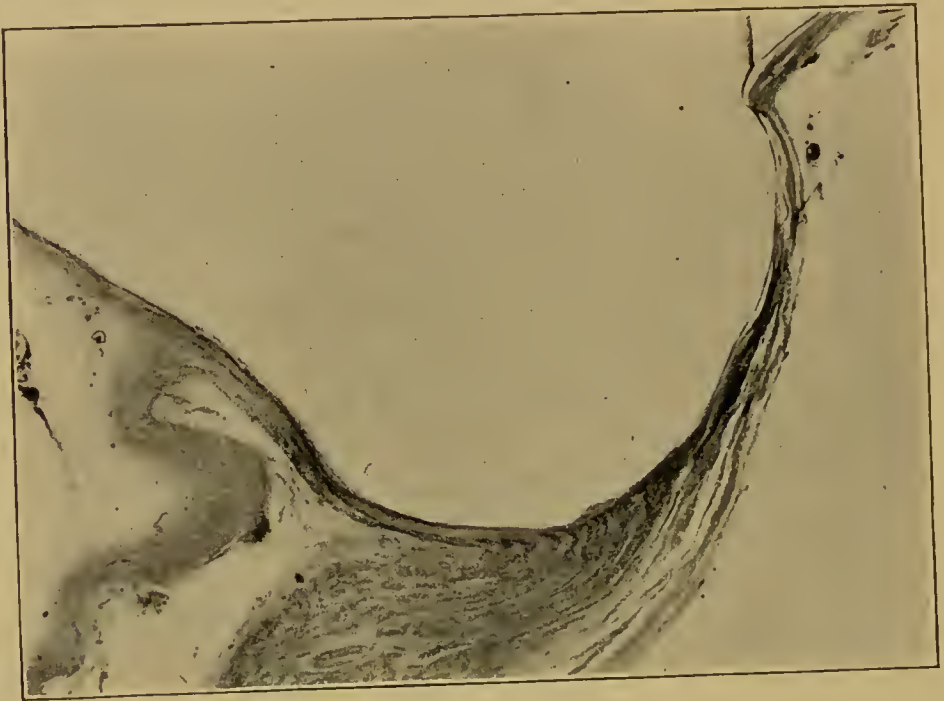
FIG. 589.—COLOBOMA OF THE OPTIC NERVE.
From a photograph by Coats.

that the majority of cases must be considered to have a normally closed fœtal cleft in so far as the nerve is concerned. When outside the nerve the proper central vessels are replaced by posterior ciliary vessels which run in the outer sheath and vaginal space (e. g. Manz) and pierce the floor of the coloboma. They are then situated in the lower segment, and the distribution corresponds with the first group of Caspar. This is the usual arrangement in microphthalmic eyes.

Caspar's second group corresponds with the nearly normal arrangement, the central vessels generally penetrating the sheath closer behind the sclerotic than usual (e. g. van Duyse). The inferior vessels may still be extra-papillary, penetrating the lower ectatic portion of the coloboma. This type of distribution was seen in Görlitz' case.

Total ectasia of the coloboma, with peripheral distribution of the

vessels—Caspar's third group—has not been examined, though one of van Duyse's cases is analogous. Neither have cases of localised ectasiæ in the coloboma: these are probably due to localised defects in the lamina cribrosa, with cystic formation, such as Görlitz found. One of van Duyse's cases nearly approaches this condition.

Actual defect in the inferior part of the nerve itself is most nearly approached in one of Bock's cases, and Ginsberg describes a deep excavation wholly limited to the papilla. Bach represents a connective-tissue cone projecting into the vitreous.

Elschnig has given an exhaustive description of the anatomical conditions in five cases of coloboma at the disc, two of which had rudimentary cysts. The most important original observation which he
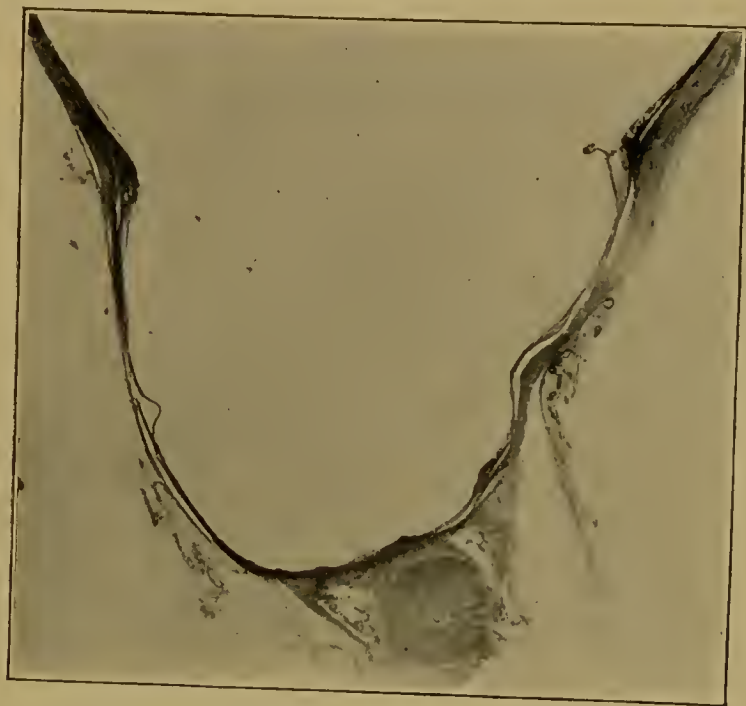
FIG. 590.—COLOBOMA OT THE OPTIC NERVE.
From a photograph by Coats.

makes is the ingrowth of retina—one or both nuclear layers—around the edge of the lamina vitrea at the disc; it persists as a pocket of rudimentary tissue separating Bruch's membrane from the choroid proper. He considers that typical, *i. e.* inferior, coloboma is due to faulty closure of the fœtal cleft when retina is absent over the affected area; too little stress is perhaps laid upon the possibility of later degeneration and atrophy of the retina. Atypical colobomata are explained by defective development of the mesoblastic tissue which forms the choroid and sclerotic, and this is itself caused by an active over-proliferation of the lips of the secondary optic vesicle into the mesoblast. This suggestion was originally made by Kundrat. (*See* also "Congenital Crescent.")

I have described a coloboma of the optic nerve in a case of microph-

thalmia associated with orbital encephalocele (Parsons and Coats). There can be no doubt that in this case the cyst invading the nerve is a true "coloboma of the nerve-sheath," not an excavation of the nerve proper (Figs. 591—596). On each side the sclera and choroid come to their normal terminations. This is especially well seen on the temporal side, where the intervaginal space gives a good rallying point. Just within it the sclera terminates in a sharp promontory; the choroid ends in the same position, and the retina a little farther in, being dragged round into the excavation for a short distance. On the nasal side the intervaginal space is left open and therefore does not furnish so good a point for orientation; but the lamina cribrosa gives the indication required. On this side also the sclera, choroid, and retina end in prac- tically normal relations to one another. There is therefore no coloboma outside the normal limits of the porus opticus. It is, in fact, that small por- tion of the scleral promontory which lies over the termination of the inter- vaginal space and to the inner side of that spot which has given way, or perhaps more properly has never been normally formed.

From the above description it will be recognised that many so-called colobomata of the optic nerve are really circumscribed choroidal colobo- mata or commencing orbital cysts, and that an actual defect in the nerve does not exist: it is impossible from the ophthalmoscopic picture to determine the anatomical condition of the nerve and its sheath (E. v. Hippel).

FIG. 591.—MICROPHTHALMIA, ETC.
Parsons and Coats, Brain, xxix. General view of the globe to show the two cysts, one at the junction of the nerve with the globe, the other involving the nerve itself. The figure also shows a piece of the dura mater of the encephalocele inseparably adherent to the globe.

Stock and Szili Jnr. have described a case in which the papilla and the whole surrounding area of sclera, choroid, and retina were bodily displaced backwards, so that a sort of staphyloma posticum verum was formed.

All the abnormalities found in the nerve entrance in my case follow from this giving way of the sclera at its margin. Since the bulging occurred to the inner side of the termination of the intervaginal space, the latter is not displaced as a whole, though spread out over the surface of the cyst. Its anterior blind end especially retains its normal relations. On the other hand, since the bulging is to the temporal side of the nerve itself, the latter becomes displaced as a whole over to the nasal side. In the normal papilla the lamina cribrosa arises from the area in ques- tion, but in the present instance it has not shared in the bulging, but has been displaced as a whole to the nasal side; and since the relations of the nerve and sclera remain normal on that side, the lamina becomes slewed round in the process, so that the surface of the papilla comes to look temporal-wards. Theoretically there should be a connection between the papilla and the retina on the temporal side; and in fact

some greatly distorted remains of retina are to be found in the cup, but owing to the great distension they have in places become completely atrophic, so that no continuous nervous layer is to be traced. Corresponding with this fact the nerve-fibre layer of the retina is highly atrophic everywhere on the temporal side but well preserved on the nasal.

The nerve has not simply been displaced by the cystic swelling, it has also been hollowed out; that is to say, it does not simply run over the wall of the cyst in the form of a cord, but has been spread out over
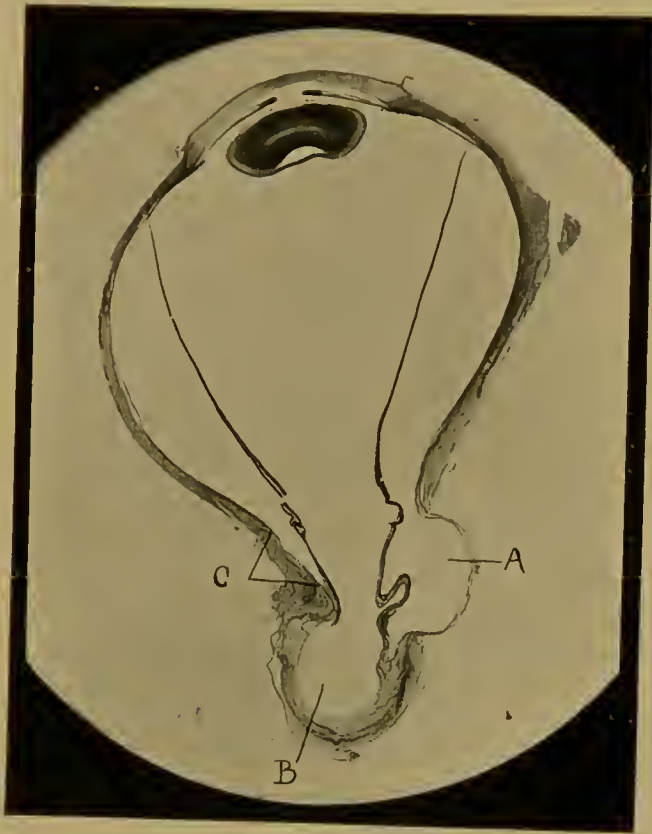
FIG. 592.—MICROPHTHALMIA, ETC.

Parsons and Coats, Brain, xxix. Section of the whole eye to show general relations. All anterior parts of the globe are normal. The shape of the lens is due to shrinkage in formalin. The detachment of the retina is also artificial. A. Thin-walled ectasia on the nasal side of the nerve. B. Coloboma of the nerve entrance. C. Position of the macular coloboma.

a large area of its wall. Hence in any given section, in addition to the thin nerve which runs round the nasal side of the cyst, transversely cut nerve-fibres are found for a considerable distance round towards the temporal side, and in peripheral sections the nerve has the appearance of being split up its centre. These transversely cut fibres are merely fibres mounting over the wall of the cyst to reach the lamina at some point above or below the plane of section; none of them enters the globe on the temporal side. It will be noted, therefore, that although the nerve is excavated, there is nothing analogous to a glaucomatous

cup. The nerve is hollowed out by invasion from the side, not by pushing back of the lamina cribrosa. The lamina, as before stated, is not involved in the bulging, but merely displaced bodily to the nasal side and slewed round so as to face temporally; it has no convexity backwards.

Together with the process of distension of the sclera there has gone on a process of thickening of its fibrous tissue. Hence the fibrous wall of the cyst, in spite of its considerable size, is not thinned but very considerably thickened. In this thick pad of connective tissue which
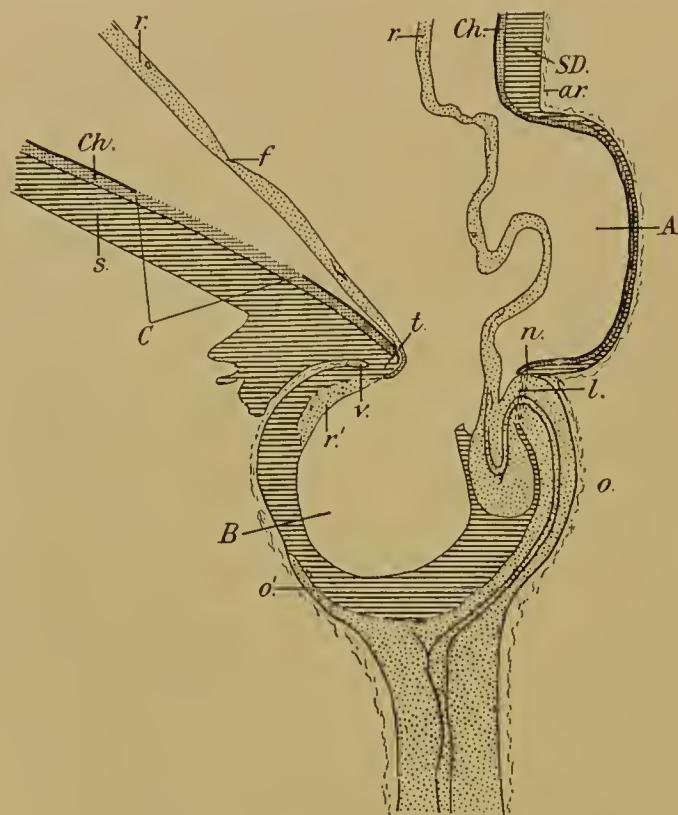
FIG. 593.—COLOBOMA OF THE OPTIC NERVE.

Parsons and Coats, Brain, xxix. Diagram of the posterior part of the globe as reconstructed from serial sections. A. Ectasia on the nasal side of the nerve. B. Coloboma of the nerve entrance. C. Macular coloboma. ar. Arachnoid lining of the encephalocele. S.D. Sclera and dura of the encephalocele inseparably united. s. Sclera. Ch. Choroid. r. Retina. f. Fovea. n. Nasal side of porus opticus. t. Temporal side of porus opticus. o. Optic nerve. o′. Tongue of optic nerve consisting of fibres mounting over the ectasia to pass through the lamina at a different level. l. Lamina cribrosa. r′. Remains of retina within the fibrous tissue lining the coloboma. v. Intervaginal space not displaced with the nerve, but retaining its normal relations to the ending of the sclera and choroid.

lines the cup a few distorted remains of retinal tissue are found on the temporal side. These may represent a slight degree of the extra-ocular cyst containing retina so commonly associated with microph-thalmia.

The nerve is atrophic but well formed. The central vessels pass up the middle and enter the globe as usual in the centre of the lamina cribrosa.

It will be seen that colobomata of the optic nerve fall usually into one of three classes. The most common are colobomata of the choroid reaching up to the nerve, and are therefore not true defects of the nerve itself. When these become ectatic the lower border of the nerve becomes displaced upwards and backwards, so that the surface of the papilla comes to face downwards, exactly as in my case it came to face temporally. Naturally in such cases the dural sheath and intervaginal space go with the nerve and are not involved in the coloboma (Manz,
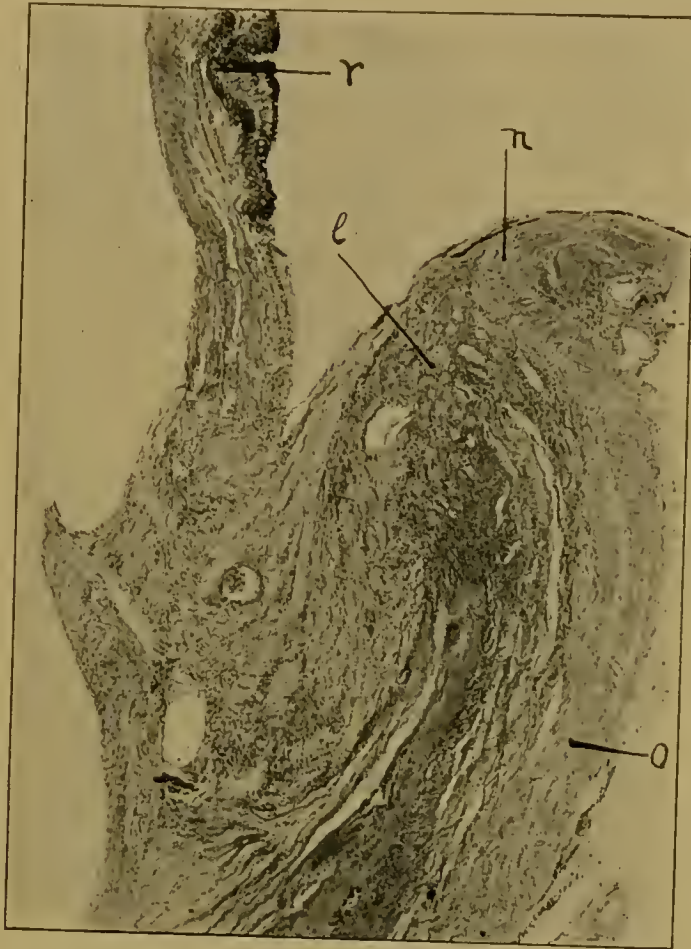
FIG. 594.—COLOBOMA OF THE OPTIC NERVE.
Parsons and Coats, Brain, xxix. Nasal side of the coloboma of the nerve to show the manner of entrance of the nerve. *o*. Nerve curving strongly round the nasal side of the coloboma. *n*. Ending of the sclera and choroid on the nasal side of the nerve. *l*. Lamina cribrosa. *r*. Retina.

Bock, Görlitz, Marshall, Knapp, Tschemlossow). The second form includes cases in which a pocket of retina is snared off just at the lower edge of the papilla, and projects into the sclera (Liebreich, da Gama Pinto, Manz, Bach (Case 1), E. v. Hippel). Usually, if large enough to appear externally it comes out below the dural sheath, so that in this case as in the last the vaginal space is not interfered with, but is displaced bodily with the nerve. Insensible gradations are found between this type and the well-known cases of microphthalmia with extra-ocular

cysts containing distorted retina. These two forms of coloboma of the nerve may be combined, and both have been found in the condition described by Fuchs and known as inferior conus—a condition which is congenital and usually associated with a considerable degree of amblyopia ; a third and much rarer form of coloboma is an actual defect of the nerve itself, the lamina cribrosa being imperfectly formed (Bach (Case 5), Görlitz, Ginsberg).

My case differs to some extent from all of those described. In the

FIG. 595.
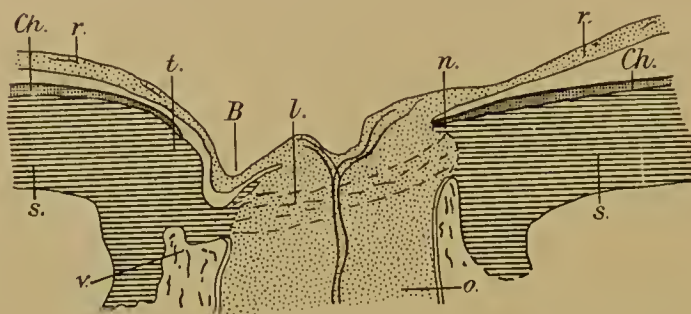
FIG. 596.
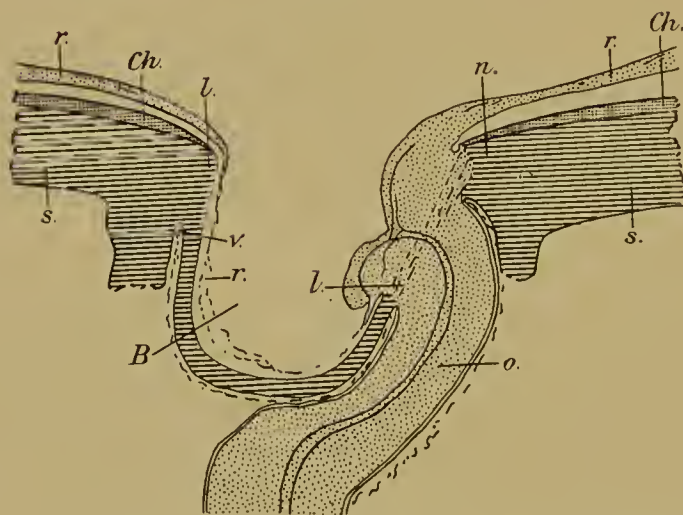
FIGS. 595 AND 596.—COLOBOMA OF THE OPTIC NERVE.

Parsons and Coats, Brain, xxix. Diagrams to show theoretical stages in the formation of the coloboma of the nerve. Lettering the same as in Fig. 593. Fig. 595 shows the junction of the sclera, with the lamina cribrosa commencing to bulge backwards into the intervaginal space. Fig. 596 shows a further stage of the same process. The nerve is being carried over to the nasal side, and the lamina cribrosa and surface of the papilla are being slewed round so as to face temporally. The ending of the intervaginal space remains in its normal position. The connection between the temporal side of the papilla and the retina is becoming greatly thinned.

first place the position of the coloboma is quite peculiar, viz. on the temporal, not on the lower, side of the papilla. Again, the choroid is not defective. It is the point of junction of the sclera with the lamina cribrosa which has become ectatic. The bulging has therefore taken place to the inner side of the intervaginal space, and the latter has not

been displaced with the nerve but has retained its normal position. The theoretical stages through which this has come about are shown in the diagrams (figs. 595, 596). Fig. 593 represents the actual state of affairs found. The only previous reference to such a condition is contained in a paper by Elschnig on inferior conus (Case 5). He found the tissues between the sclera-dura and the nerve ectatic, bulging into the vaginal space, but as this occurred in a very highly myopic globe it is doubtful whether the condition was congenital or due to myopic expansion.

The case furnishes a good example of a central or macular coloboma (Figs. 592, 593, C). As in the coloboma on the nasal side of the disc, so here, there was no actual gap in any layer. In the retina there was even an imperfectly formed but quite recognisable fovea. This has not been previously found in a macular coloboma. The most defective layer was the pigment epithelium. It was present only in islands and had entirely lost its pigment. It should be noted that neither here nor in the other colobomata was there the least evidence of old or recent inflammation. Indeed, the absence of all adhesion between the retina and the choroid is direct proof to the contrary. Hence the case adds to the already considerable body of evidence against Deutschmann's theory that all colobomata are due to inflammation in early foetal life. There was also no bulging of the ocular tunics. It seems evident therefore that the adhesion between retina and choroid, the extreme atrophy and distortion of these layers, and the deep excavations which have been usually found in pathological examinations of macular (and other) colobomata are secondary phenomena, due to subsequent inflammation, or to stretching and giving way of a weak part of the globe. It is highly probable that they were not present in this instance because the eye was obtained from an infant, and therefore before secondary changes had occurred. Confirmation of this view is obtained from a case of Pause's in which the retina and choroid were both quite intact over a coloboma of the choroid, while the pigment epithelium was present but deprived of its pigment. The case therefore closely resembles mine, and it occurred in a child which died at birth. Depigmentation of the pigment epithelium has also been noted by Bock and others over typical colobomata of the choroid. The changes most commonly found in macular colobomata are described in the papers of Hess, Bock, Deyl, and v. Duyse.

It seems evident that in this case the abnormalities present in the eye were not independent of the orbital encephalocele (v. p. 884). Had the colobomata been of the ordinary type, it might have been possible to suppose that they were one expression of a general tendency towards the formation of congenital abnormalities, while the brain tumour was another expression of the same tendency, just as, for instance, super-numerary digits on the hands and feet are frequently associated yet not dependent the one on the other. But in view of the fact that the brain masses in the orbit directly pressed upon and flattened the globe, and since two at least of the colobomata were of quite an atypical variety, it seems much more likely that they stood in the relation of cause and effect. Moreover microphthalmia with colobomata has been found

associated with contraction of the orbit from hydrocephalus (Rindfleisch, Hans Virchow).

A possible explanation would be that the apparently isolated mass of brain substance had been snared off at an early period of fœtal life, and had interfered with the proper budding out of the primary optic vesicle, or had even been derived from a portion of brain substance which should have gone to the formation of the vesicle. It seems highly improbable, however, that if this had been so the globe would have been so well formed, especially in its anterior parts. Since there is no defect below, either in the nerve or retina, it is evident that a secondary optic vesicle also formed and closed in the usual manner. The defects in the globe were therefore caused by the pressure of the growing brain masses on the growing secondary optic vesicle.

*CASPAR.—Dissertation, Bonn, 1887. *SAEMISCH, CASPAR, AND KRUGER.—Festschrift f. v. Helmholtz, 1891. BLESSIG.—K. M. f. A., xxvii, 1889. NIEDEN.—A. f. A., viii, 1879. REMAK.—C.f. A., viii, 1884. FEHR.—C.f. A., xxiv, 1900. SCHÖLER.—Bericht ü. d. Sch. Anstalt, 1875. WIETHE.—A f. A., x, 1881. SCHNABEL.—Wiener med. Blätter, 1884. STOOD.—K. M. f. A., xxii, 1884. *BOCK.—Die angeb. Colobome des Augapfels, Wien, 1893. BECKER.— In G.-S., v, 1877. BAYER.—Prager med. Woch., 1881; Z. f. Heilkunde, iv, 1883. v. REUSS.—Ophth. Mittheil., Wien, 1886; in Rumschiewitsch, A. f. O., xxxvii, 4, 1891. HEGG.—Rec. d'O., 1892. GINSBERG.—C. f. A., xx, 1896. PFANNMÜLLER.—Dissertation, Bonn, 1894. EVERSBUSCH.—K. M. f. A., xxiii, 1885. TERESCHKOWITSCH.—A. f. A., xli, 1900. WEISS AND GÖRLITZ.—A. f. A., xxxiii, 1896. *GÖRLITZ.—A. f. A., xxxv, 1897. BENSON.—Jl. Dublin Med. Soc., 1882. v. AMMON.—v. Ammon's Zeitschrift, i, 1831. LIEBREICH.—A. f. O., v, 2, 1859. HESS.—A. f. O., xxxviii, 3, 1892; A. f. A., xli, 1900. VAN DUYSE.—A. d'O., xvi, 1896. MANZ.—A. f. A., xxiii, 1891. *BACH.—A. f. O., xlv, 1, 1898. *ELSCHNIG.—A. f. O., li, 3, 1900; Denkschriften d. k. Akad. der Wissensch. in Wien, lxx, 1901. KUNDRAT.—Wiener med. Blätter, 1886. *VAN DUYSE.—A. d'O., xi, 1891; Ann. d'Oc., xcii, 1884; Rev. gén. d'O., 1897; Encyclopédie franç., ii, Paris, 1905. *E. v. HIPPEL.—In G.-S., 1900. PARSONS.—T. O. S., xxi, 1901. WERNER, THOMSON, AND BALLANTYNE.—T. O. S., xxiii, 1903. MARSHALL.—R. L. O. H. Rep., xv, 1899. KNAPP.—A. f. A., xliii, 1901. TSCHEMLOSSOW.—In Nagel's Jahresbericht, 1901. DA GAMA PINTO.—A. f. A., xiii, 1884. RINDFLEISCH.—K. M. f. A., xxxii, 1894. HANS VIRCHOW.—v. Kölliker's Festschrift, Leipzig, 1887; in Rindfleisch, A. f. O., xxxvii, 3, 1891. *PARSONS AND COATS.—Brain, xxix, 1906. STOCK AND SZILI JNR.—K. M. f. A., xliv, 1906.

Congenital crescent (inferior crescent, inferior staphyloma, conus nach unten, cône inférieur, cône sous-papillaire, Fuchs's coloboma). In this condition the disc, often unduly small, is horizontally oval, the lower limit being rectilinear, separating it from a white crescentic area. The cone may be irregular, triangular, rarely vertically oval. The physiological cup is often directed downwards, the neighbouring part of the fundus may be poor in pigment (Szili).

Liebreich (1859) first conjectured a possible connection with choroidal coloboma. Jaeger (1861) considered that the inferior crescent was due to defective closure of the fœtal cleft, and this idea was adopted by Schnabel (1874). Both Jaeger and Schnabel described congenital crescents on the temporal side in the new-born and in high hypermetropes. Fuchs (1882) laid still further stress upon the necessity for distinguishing between the congenital crescents and the acquired, which were due to myopic choroidal atrophy. He pointed out the frequency of errors of refraction and very defective vision. Wollenberg (1889) emphasised strongly the occurrence of inferior crescents in the insane. He found them in 1·3 per cent. of insane patients, as opposed to 0·9 per cent. of eye patients (Vossius). The

difference is not sufficient to base any revolutionary principle upon, though it is noteworthy that the percentage is increased to 4·7 in congenital psychoses (hysteria, idiocy, epilepsy). Elschnig (1900) examined 481 eyes—75 emmetropic, 202 hypermetropic, 204 myopic—and found temporal crescent in 217, inferior in 25, nasal in 19, superior in 2 ; he found temporal coloboma in 9, inferior in 14, superior in 1 : by far the most of these anomalies were in myopic eyes. Elschnig's differentiation of conus and coloboma must be borne in mind in considering these statistics (*v. infra*).

Vossius found the congenital crescent situated as follows in 111 cases : below, 75 (67 per cent.) ; down and in, 8 (7·3 per cent.) ; in, 9 (8·1 per cent.) ; up, 5 (4·5 per cent.) ; up and out, 8 (7·2 per cent.) ; down and out, 6 (5·4 per cent.).

Elschnig distinguishes between a conus and a coloboma. The principal criterion is the level of the crescent : if the white area near the disc is at the same level as the disc, it is a conus ; if it is ectatic, it is a coloboma. On the other hand, the absence of ectasia does not eliminate the possibility of a coloboma.

Inferior crescent has been seen accompanied with typical choroidal and also macular coloboma.

Salzmann (1893) made the first anatomical examination of an inferior crescent, though it had not been seen ophthalmoscopically. The pigment epithelium and the inner layers of the choroid were absent, whilst the retina was duplicated, the outer layer being scarcely recognisable. The inner layer showed defective development of the outer retinal layers. The author regarded the condition as a feebly developed coloboma of the choroid. Elschnig doubts whether Salzmann's case was a true conus. He examined 22 cases of temporal or infero-temporal crescents (1901), as well as five colobomata at the disc, 1 inferior conus, and 1 internal conus, a condition not previously described (1900). The inferior conus nearly resembles the temporal conus of myopic eyes. The membrana vitrea and pigment epithelium are retracted from the edge of the disc so as to leave the sclerotic exposed, covered only by rudimentary choroid : there is peculiarly little " intermediate tissue " (*v.* Vol. II, p. 655) in the inferior conus. A difference is seen in the distension of the vaginal space on the side of the inferior crescent, and the sclera, choroid, and retina are all thinned. Elschnig concludes that inferior conus and probably coloboma and crescents in other directions are not to be explained as remnants of the fœtal cleft. They are the expression of stretching of the membranes of the eye, due to defective development : already during fœtal life equilibrium between the elasticity of the membranes and the intra-ocular pressure is probably attained, but may be subject to change in extra-uterine life. The abnormal expansibility of the wall is due to maldevelopment because the relative thinning is too great to be accounted for by the degree of stretching. The frequency of the anomaly in the lower part is determined by the position of the fœtal cleft, but all types of conus and coloboma of the optic nerve are caused by abnormal outgrowth of the lips of the secondary optic vesicle in the fœtal cleft or at the margin of the disc, inducing defective

development in the mesoblastic tissue which gives rise to the choroid and sclerotic. Elschnig is inclined to attribute all crescents, including myopic, to congenital defect which may become intensified subsequently.

LIEBREICH.—A. f. O., v, 2, 1859. JAEGER— Ueber die Einstellungen des dioptr. Apparats im mensch. Auge, Wien, 1861. SCHNABEL.—A. f. O., xx, 2, 1874; Wiener med. Woch., 1876; Wiener med. Blätter, 1884. SCHNABEL AND HERRNHEISER.—Z. f. Heilkunde, xvi, 1895. FUCHS.—A. f. O., xxviii, 1, 1882. BENSON.—Dublin Jl. of Med. Sc., 1882. SZILI.—C. f. A., vii, 1883. WOLLENBERG.—Charité Annalen, xiv, 1889. VOSSIUS.— K. M. f. A., xxiii, 1885. *VAN DUYSE.—Ann. d'Oc., xci, 1884; Encyclopédie franç., ii, 1905. *E. V. HIPPEL.—In G.-S., 1900. SALZMANN.—A. f. O., xxxix, 4, 1893. *ELSCHNIG. —A. f. O., li, 3, 1900; Denkschriften d. k. Akad. d. Wissenschaften in Wien, lxx, 1901.

Coloboma of the vitreous.—This condition can only be studied anatomically, best after long hardening in Müller's fluid (Bock). Early observations by v. Ammon, Arnold, Stellwag, Hannover, Ecker, are recorded by Manz. There is an indentation in the lower part of the vitreous, which may be total, involving the whole meridian, or partial—anterior or posterior. The depth varies greatly. The cleft is filled with vascular connective tissue, or in one case in a pig, with a fold of retina (Hess). Bock records other cases, but the most exact anatomical investigation is by Hess. He found the vitreous quite normal; in one case the subhyaloid cells were increased. The edges were covered by a delicate hyaloid membrane.

MANZ.—In G.-S., ii, 1876. HESS.—A. f. O., xxxviii, 3, 1892. BOCK.—Die angeb. Colobome des Augapfels, Wien, 1893.

Coloboma of the lens.—Records of coloboma of the lens are comparatively rare, but the condition is probably often missed, especially in its slighter forms. Kämpffer (1899) collected 132 cases: he defines the coloboma as a congenital defect in the edge, with loss of substance, true or false, the lens being otherwise normal in shape. The indentations may be single or multiple. Three types are somewhat indefinitely distinguished: (1) simple indentation; (2) a straight line, with or without conical humps upon it; (3) projection to a point (Bock, Doyne), which may have an indentation at the tip (Bock). Two deep indentations close to each other (Meyer) are rare.

FIG. 597.—COLOBOMA OF LENS. Marcus Gunn, T. O. S., xxiv. Showing coloboma upwards, with defective development of the suspensory ligament.

The coloboma is usually in the typical direction, downwards or down and slightly in or out. Colobomata in other directions are: up (5 to 41 inferior, Bock)—Knapp (1862), Schaumberg (1882), Rogman (1898); in—Baas, Vossius (1893), Kämpffer, Hess (1896); up and in—Hess (1892) with corresponding coloboma of iris and choroid; up and out—Narkiewicz-Jodko (1879), Schaumberg (1882) with bilateral upward corectopia; out—Schiess-Gemuseus (1871), Lang and Treacher Collins (1890) with corresponding coloboma of iris, Kämpffer (1893); down and out—Cissel (1890), Christen (1894); down and in—Cissel (1890) in the other eye.

Kämpffer gives four grades—notch, triangle, ellipse, segment ; he calls the edge of a dislocated lens a false coloboma, and this may easily be mistaken for the fourth grade.

The condition of the suspensory ligament is important, but the records do not afford very trustworthy evidence, since it is only with the greatest care that the normal filaments can be seen. Both complete absence and full development have been reported, the latter even in large inferior colobomata (Schiess-Gemuseus, Cissel), and in the cases of Becker and Marcus Gunn. Bock found fibres in two cases and noted their absence in four others : Christen saw them in one eye and not in the other.

The coloboma is usually unilateral: it is equally distributed between the two sexes (Kämpffer). Myopia is common (24 times in 82 eyes, Kämpffer), which Kämpffer is inclined to attribute largely to increased curvature of the lens from relaxation of the zonule. Knapp noted lenticular astigmatism. In Chibret's case the lower part of the pupil was aphakic with a refraction of $+$ 12 D, without dislocation of the lens.

Concomitant abnormalities are most frequently coloboma of the iris and choroid. Atypical coloboma of the iris is noted by Lang and Treacher Collins, Christen, and Hess. Incomplete development of the iris is described by Bronner and Baas, and corectopia to the same side by Schaumberg and Kämpffer ; the latter records persistent pupillary membrane five times and iridodonesis five times. Simultaneous ectopia of the lens is recorded by Bowman, v. Ammon, Marcus Gunn, Heyfelder, and Marple. Various forms of cataract have been observed : nuclear, central, anterior and posterior cortical, total juvenile and senile, posterior polar, partial persistent posterior lens sheath, and localised opacity in the colobomatous area. The cases of persistent vascular sheath of the lens, both anterior and posterior, are important from the pathogenic point of view, especially the cases of E. Meyer, Baas, Vossius, and Hess. Hess, in discussing Meyer's case, first propounded the theory that the coloboma is due to abnormally long persistence of some of the vessels of the lens sheath ; these may later disappear partially or completely. In the case described by Baas, with a nasal coloboma, there was an apparent posterior synechia, made up of a cone of fibrous tissue springing from the lesser circle and passing backwards to invaginate the lens slightly. Vossius' case was microphthalmic : the lens was opaque and reniform, with the hilum directed nasally ; a delicate vascular membrane invaginated the cleft and spread over the back of the lens, one of the vessels being derived from a ciliary process.

Anatomical investigations have mostly been carried out on cataractous lenses by Bock and Hess, the latter in a microphthalmia.

BRESGEN.—A. f. A., iv, 1874. BOCK.—Die angeb. Colobome des Augapfels, Wien, 1893. *KÄMPFFER.—A. f. O., xlviii, 3, 1899. DOYNE.—T. O. S., xi, 1891. KNAPP.—A. f. O., viii, 1862.—SCHAUMBERG.—Dissertation, Marburg, 1882. ROGMAN.—A. d'O., xvii, 1897. BAAS.—K. M. f. A., xxxi, 1893. VOSSIUS.—B. z. A., ix, 1893. HESS.—K. M. f. A., xxx, 1892 ; B. d. o. G., 1892 ; K. M. f. A., xxxiv, 1896 ; A. f. O., xlii, 3, 1896. NARKIE-WICZ-JODKO.—C. f. A., ii, 1879. SCHIESS-GEMUSEUS.—K. M. f. A., ix, 1871 ; A. f. O., xxxi, 4, 1885. LANG.—T. O. S., x, 1890. TREACHER COLLINS.—T. O. S., xiii, 1893. CISSEL.—

K. M. f. A., xxviii, 1890. Christen.—A. f. A., xxix, 1894. Becker.—Atlas, Plate III, 1878. Marcus Gunn.—T. O. S., ix, 1889; xxiv, 1904. Chibret.—Rev. gén. d'O., 1893. Bronner.—T. O. S., xvii, 1897. Bowman.—R. L. O. H. Rep., v, 1865. Marple.—New York Ear and Eye Infirmary Rep., 1894. Leber.—A. f. O., xlviii, 1889. Hess.—A. f. O., xxxiv, 3, 1888. E. Meyer.—B. d. o. G., 1892; Rev. gén. d'O., 1893. Clark.—T. Am. O. S., 1894. Dunn.—A. f. O., xxv, 3, 1896. Bach.—A. f. O., xlv, 1, 1898. Toldt.—B. z. A., xliv, 1900. Morton.—T. O. S., xxi, 1901.

Coloboma of the zonule of Zinn.—The investigations of Bock have demonstrated the frequent absence of the zonule in the region of a coloboma of the lens: purely clinical statements must be accepted with reserve. The defect is usually triangular with the base at the ciliary body, and the fibres may be present at the margins of the coloboma, where they are often thicker than normal. They are also absent in coloboma of the ciliary body. The fibres are frequently irregularly arranged. It is said that the zonule may be normal, with absence of the ciliary processes or very defective development of the ciliary body.

Bock.—Die angeborenen Colobome des Augapfels, Wien, 1893.

The pathogenesis of colobomata.—*A priori* the relatively extreme frequency of typical, *i. e.* inferior, colobomata, irresistibly prejudices opinion in favour of some interference with the normal closure of the fœtal cleft. It is not surprising, therefore, that this theory was long accepted, almost without discussion except in minor details. It was propounded by v. Ammon (1831), who described a colobomatous eye in pre-ophthalmoscopic days. It was supported by Remak, Schöler, and v. Kölliker, and was adopted by Manz, Bock, and Hess, finally receiving unlooked for experimental confirmation in the researches of E. v. Hippel (1903). It may therefore be said still to hold the field in spite of the almost insuperable difficulties which increased knowledge has revealed.

The earlier views were summed up by Manz (1876), who pointed out the three factors which he considered essential: (1) defective closure of the fœtal cleft; (2) abnormal development of the surrounding mesoblast, the precursor and progenitor of the choroid and sclerotic; (3) expansion and ectasia of the cicatricial tissue under the influence of the intra-ocular pressure. The cause of the defective closure was considered to be deficient retrogression of the invaginating mesoblast, due probably to over-vascularisation and undue organisation. Coloboma of the iris was explained by interference with the proper forward growth of the lip of the optic vesicle and union with the iridic mesoblast owing to late or defective closure of the cleft. Coloboma of the iris without coincident coloboma of the choroid was explained by subsequent complete closure and obliteration of the choroidal cleft. *Mutatis mutandis*, the same argument was applied to coloboma of the choroid without coloboma of the iris.

Further investigations revealed facts which militated strongly against this simple and attractive theory. The chief of these are: (1) the occurrence of atypical colobomata, *i. e.* colobomata directed other than downwards; macular coloboma should be included in this

category; (2) the presence of both layers of the secondary optic vesicle over the colobomatous area. So potent were the arguments derived from the study of these difficulties that Deutschmann (1881) had recourse to the intra-uterine inflammatory theory, and was supported by a large following, including Höltzke, Thalberg, Tartuferi, Picqué, Schweigger, de Lapersonne, and even for a time van Duyse (1886). Ginsberg (1896), indeed, went so far as to say that colobomata could only be explained by a theory which absolutely renounced the intervention of the foetal cleft.

These arguments must now be weighed more in detail. It is clear that atypical colobomata cannot be elucidated by a straightforward application of the theory of arrested development as expounded by Manz. Deutschmann's theory would seem to afford a satisfactory explanation, but more minute investigation tends to discount it seriously. It is open to the following prime objections: (1) there was no sign of inflammatory processes in Deutschmann's case, nor can the slightest sign of inflammation be observed in colobomata examined in the foetus or in the newborn (see especially E. v. Hippel, 1903); per contra it may be alleged that little is known of the signs of "inflammation" in the broad sense (v. p. 772) in the foetus, and that its results may be devoid of the signs commonly associated with inflammation; these are usually found in old cases, and are almost certainly secondary; (2) it cannot be truly described as a "sclero-choroiditis" in any case, since the sclera and choroid are not differentiated at this period of foetal life; (3) inflammation localised to the foetal cleft, and often bilateral, is difficult to accept; (4) the abnormality is often hereditary (e.g. Weyert—ten colobomata in three generations, Pflüger, Pfannmüller, de Wecker, E. v. Hippel) and associated with other congenital anomalies.

Leber and Addario, whose observations on intra-uterine inflammation are of the utmost importance (v. Vol. I, p. 53, Vol. III, p. 773), consider that it may undoubtedly cause arrest of development of the whole eye or a part; in the absence of trauma it may be the principal or even sole cause. The disappearance of the signs of inflammation is not unknown in later life. Pichler, again, invokes the deleterious effect upon the highly differentiated cells of the optic vesicle of malnutrition or toxins derived from the mother. Such toxins manifest their activity most upon mesoblastic tissues. The toxic effects of tubercle, alcohol, and especially syphilis, have been exhaustively considered by E. Fournier. The idea that they may so interfere with development as to lead to a sort of atavism has its fascinations. All that can be said at present is that these theories are purely conjectural, whilst the possibility of their affording a complete explanation cannot be denied. The scientific attitude, as usual, is one of enlightened agnosticism.

Macular coloboma is a specific instance of atypical coloboma of the fundus which raises points of unique interest. In the early days it was held that the macula develops in the foetal cleft, and as this theory was inconsistent with the temporal situation of the fovea it was said that the eye rotated 90° during development (v. Kölliker, Manz). Vossius (1883) advanced as proof of rotation the entrance of the

central vessels into the optic nerve in the infero-lateral quadrant (man, calf, lamb, cat), and the primary situation of the levator palpebræ and superior rectus along the lateral wall of the orbit (fifth to sixth month). As regards the first point the exact site of entry, whether slightly temporal or nasal, is notoriously inconstant, but it is usually nasal : as regards the second it is a proved error of observation (Deyl, Henckel). v. Kölliker and Manz held that the fœtal cleft extended a short distance above the optic disc, and that the fovea developed in this situation. Rotation in the sense adopted by Vossius would then entail a nasal site for the macula ; moreover, it has been proved that the cleft does not extend above the disc. Finally, the theory may be said to have been given its *coup de grace* by the conclusive proof that the fovea is not developed in the fœtal cleft (Chievitz).

Some cases of macular coloboma bear such distinct resemblance to patches of choroiditis, and are accompanied by other such patches elsewhere in the fundus of the same or the other eye (*e. g.* Lister) that pre- or post-natal inflammation seems the simplest explanation. At the same time, they submit equally well to the theory of arrested development as applied to atypical colobomata in general.

Macular colobomata are attributed by Deyl and Lindsay Johnson to telangiectases in the choroid : these interfere with proper development, but may subsequently disappear. The theory is purely conjectural.

The key to the aplasic theory of atypical colobomata is afforded by the discovery of an atypical, subsidiary fœtal cleft, in addition to the normal one. v. Ammon (1858) found three examples in the chick and the sheep of atypical choroidal fissures associated with a normal one, twice upwards, once outwards. He refers to two similar observations by Warnatz (lateral) and Emmert (amphibian). The observation would seem to be placed beyond dispute by a double fœtal cleft in a calf embryo described by van Duyse. The embryo was 13·5 mm. long ; the normal cleft was situated down and in and exactly resembled that in the other eye ; the accessory cleft was directed down and out, and extended from the equator forwards, where it is fused with the other. The mesoblast in the normal fissure showed the usual arrangement, passing in towards the lens ; that in the abnormal cleft was directed parallel to the plane of the retina. Manz (1888) did not consider that atypical coloboma formed a sufficient reason for invoking an atypical fœtal cleft—a proper attitude to adopt, since pathological observations should never be adduced as other than merely confirmatory evidence of physiological conditions. Bock considered that the cases reported by v. Ammon not only lacked microscopic proof, but were open to the interpretation that they belonged to different periods of development, and were due to rotation of the eye. This view is untenable, and in the face of van Duyse's case the occurrence of atypical fœtal clefts must be held proved, though confirmation is much to be desired.

Notwithstanding these considerations, there are many difficulties yet to be overcome. These depend chiefly upon the exact reports which have now accumulated of the elements present in the colobomatous

area. The reports show a large number in which it is stated that both layers of the secondary optic vesicle are represented. It is true that they are usually in an extremely degenerated condition and are scarcely recognisable. Moreover most of the eyes have been examined in sagittal section, whereas only frontal sections can give unequivocal evidence (E. v. Hippel). Further, observations of the eyes of any but very young subjects are open to profound errors in interpretation, owing to later inflammatory or degenerative changes (Haab).

Granted that colobomata are due to arrested or defective closure of the fœtal cleft, there still remains the question of the mechanism whereby this is brought about. The following theories have been advanced: (1) *the mesoblastic theory*, that the seat of the mischief is in the mesoblast, whether consisting of over- or under-development; (2) *the retinal theory*, that the primary seat is in the retina, which proliferates unduly; (3) *the lenticular theory*, that closure is prevented by relative abnormal development of the lens as compared with the size of the eye.

The last theory may be considered first. It was enunciated by Bach, who in one case found one eye smaller than the other. In this eye the lens filled the secondary optic vesicle, pressed against the retina, and would presumably have prevented the closure of the cleft. It is not probable that this is a common cause, if it ever has any influence.

The other theories can best be elucidated by a description of E. v. Hippel's experiments (1903). This investigator bred rabbits from a male with typical coloboma of the choroid and small colobomata of the iris and lid; the females were normal. A considerable proportion of the offspring had colobomata—112 eyes were examined at different stages of fœtal life—and 23 had coloboma. The earliest was observed on the thirteenth day: the edges of the fœtal cleft are then separated by a very narrow band of vascular mesoblast, which rapidly increases in size, so that at the fifteenth day it forms a considerable band. The cells in the lips of the optic vesicle are absolutely normal; there is not the slightest trace of inflammatory or other deleterious influence. There is then a struggle between the edges of the optic vesicle and the mesoblast; this is chiefly influenced by the amount of vitreous fluid, upon which the volume of the bulbar contents depends. If this is normal, *i. e.* if the vesicle is of normal size, the retina spreads out without folding; if it is diminished the retina becomes folded and endeavours to find space for itself by overlapping the edges. Hence duplicature of the retina at the edges of the cleft occurs in these cases (*ectropion of the retina*, Salzmann); it is most marked in the posterior part, near the equator. The pigment epithelium does not overpass the border. If the development of the vitreous still lags behind, the folding of the retina becomes more pronounced, so that convolutions are found behind the lens, or they may be pushed out of the cleft into a space which will later form an orbital cyst.

E. v. Hippel attributes the amount of secretion of vitreous fluid to the condition of the invaginated mesoblast: if this is unduly dense less fluid is secreted, and microphthalmia may be thus caused; if none is formed the condition will be so-called anophthalmia. If the mesoblast

proliferates only within the eye and the cleft is allowed to close, then microphthalmia without coloboma is produced.

Later stages show that the retina is still folded over the whole cleft, while the pigment epithelium is absent. A very small plug of mesoblast in the cleft may cause the broadest coloboma, which is determined clinically by the absence of pigment in the epithelium. In these cases, and probably in all, the pigment epithelium itself is absent.

As soon as the choroid becomes differentiated it is seen that it too stops at the edge, level with the pigment epithelium, and the same applies to the inner scleral laminæ; the outer, which are laid down later, become formed normally. Since the wall is thus thinner at this part, it is easy to understand how even the normal intra-ocular pressure may cause ectasia: thus arise ectatic colobomata and orbital cysts.

Mannhardt and others lay stress upon the presence of both layers of the secondary optic vesicle in the colobomatous area, Mannhardt concluding that the fœtal cleft closed, but a sclero-choroidal coloboma persisted. E. v. Hippel objects that (1) the eyes were cut meridianally; (2) the colobomata were very ectatic and therefore difficult to interpret; (3) the outer layer may have been the degenerated outer layer of a retinal fold, and not pigment epithelium. He points out that even in the new-born rabbit the outer layer of the duplicature consists of a simple layer of tall cells which merge at the edges into the pigment epithelium. In a case reported by Hess both layers of the vesicle were present in one part of a coloboma whilst the fœtal fissure was open elsewhere. Here the impediment to closure existed in one part only for a time (E. v. Hippel). Mannhardt has since described cases which seem to show that late fusion of the layers of the secondary optic vesicle may occur, whilst the choroidal defect persists.

It will be remembered that Elschnig, in considering colobomata and crescents at the optic disc (p. 833), concluded that there was excessive proliferation of the lips of the optic vesicle. E. v. Hippel does not think that this assumption is necessary, the excessive proliferation being on the part of the mesoblast. Atypical colobomata at the disc can be explained by duplicature of the retina on one side only of the fœtal cleft. There is, indeed, anatomical evidence of increased growth on the temporal side in man in the fact that in the new-born the fovea is already as far distant from the papilla as in the adult (Merkel and Orr, E. v. Hippel).

E. v. Hippel has found an explanation for the now discredited view that the fœtal cleft extends above the disc, and also for the inclusion of the disc in a large coloboma of the choroid. In some cases there is an anomaly of insertion of the optic nerve, so that the pigment epithelium overlaps a thin fold of optic nerve. A similar appearance has been seen in myopic eyes, and is rightly explained as a congenital abnormality (Heine).

It will have been noted that E. v. Hippel invokes an abnormally persistent and strongly developed mesoblast. As to the fate of the mesoblast which enters the eye, whether it is the essential foundation of the vitreous or not is left an open question. The point upon which stress is laid is that the future expansion of the globe is dependent rather

upon the amount of vitreous fluid secreted than upon the mass of tissue, which acts only indirectly.

E. v. Hippel's experiments were not well adapted to investigate the influence, if any, of the brain upon the origin of colobomata. So far as they went no abnormality could be seen in the condition of the lumen of the optic stalk or in the remnants of the primary optic vesicle—*i. e.* the space between the two layers of the retina. There was therefore no ground to suppose that more fluid than normal was present here (van Duyse), a theory which was primarily adduced as an explanation of perverse arrangement of the retina in congenital orbital cysts (Mitvalsky) (*v. infra*).

Neither was there any evidence that the amnion played any part (van Duyse, Pichler).

These experiments open up a wide field for future inquiry of a somewhat laborious nature. It is to be hoped that they will be pursued so as to place the matter beyond doubt.

The one ætiological factor which comes out beyond dispute is heredity. Laqueur points out the important part played by the mesoblast as the transmitter of hereditary characteristics. Whether there is also a modified atavism, a reversion to the conditions normal in birds and fishes, possibly induced by some dystrophy, must be left an open question.

Coloboma of the ciliary body is open to the same explanation as coloboma of the choroid. When only retraction of the ciliary processes is found this may be due to their being pulled backwards by ectasia in the choroidal coloboma, but it has been seen in the absence of such ectasia (Pause).

Coloboma of the iris may be explained thus: if the fœtal cleft fails to close, there is no retinal lip here and the choroid does not become differentiated; hence neither epi- nor meso-blastic elements of the iris can grow forwards. In the absence of a choroidal coloboma the explanation is more difficult. It is not due to development whilst the cleft is still open, closure being effected after its formation, since the iris is developed quite late. There is a further complication introduced by the cases in which the retinal—pigment epithelial—layer is developed, whilst the stroma is not—*i. e.* a coloboma of the mesoblastic part only. Some cases may be explained by Mannhardt's theory that the iris is pulled back by cystoid changes behind, but this has no general application. Manz found thinning of the outer layers of the choroid in a case of atypical coloboma of the iris. The iris is, however, not simply an outgrowth from the choroid. The unusual frequency of atypical colobomata in the iris must be borne in mind.

It is probable that abnormalities in the vascular sheath of the lens may account for some colobomata of the iris. The only mesoblast which enters the eye is that through the fœtal cleft; none enters with the lens (Cirincione). The tissue to form the pupillary membrane therefore grows forwards from behind, and the vascular sheath of the lens is thus everywhere continuous with the mesoblast in or inside the cleft. The pupillary membrane gets its blood supply from the circulus iridis major, the posterior sheath from the hyaloid

artery. The venous outflow from both is into cilio-choroidal vessels at the equator of the lens, and this exit must persist as long as the pupillary membrane—*i. e.* nearly until birth.

Two abnormalities are conceivable: (1) adhesion of the pupillary membrane or sheath to the lens (Plange, Seggel), (2) atypical development of the mesoblast so that firm bands unite the lenticular part with that in or within the fœtal cleft.

The first possibility has not been demonstrated in fact, though the occurrence of synechiæ of the pupillary membrane and the frequent presence of pigment deposits on the lens capsule (*v.* p. 796) are in its favour. It may be due to intra-uterine inflammation.

The second possibility is well founded, the classical example being recorded by Hess, where there was a definite band hindering the development of the iris: other cases are reported by Bach and de Vries.

Rumschewitsch attempts to explain coloboma by the lack of union of the mesoblastic with the epiblastic elements of the iris. It is difficult to imagine why this is effected or how it acts.

The intra-uterine inflammatory theory has been invoked, especially for atypical colobomata. It is supported by the frequent signs of inflammatory disturbance which are met with, but it is difficult to apply it to bilateral cases.

Coloboma of the lens has been explained in various ways. The earliest theory was enunciated by v. Oettingen, and was adopted by Becker; according to it there is a defect in the zonule of Zinn or deficient tension in certain fibres of the suspensory ligament. This will scarcely account for more than the slighter notches. Heyl considered that parts of the lens were insufficiently nourished and therefore developed defectively owing to deficient blood supply to the vascular sheath. The opposite and more probable view was advanced by Hess, viz. that the vessels in the vascular sheath persisted too long, so that growth of the lens was prevented by local pressure. Since the sheath persists until late in fœtal life deep indentations may be produced by dense vascular bands. The cases of Meyer (with two notches) and Baas can be best explained on this theory. Broad linear colobomata are more easily accounted for by defective development of the zonule (Kämpffer).

Typical coloboma of the lens is usually associated with coloboma of the choroid, and this has been considered to be the cause by Manz and others. In reality this theory does not involve any essential difference from that of Hess. It depends upon the persistence of vascular connective tissue, which, however, in this case remains in communication with the fœtal cleft.

Deutschmann's intra-uterine inflammatory theory has been applied to the lens without sufficient grounds by Kämpffer. Bach considers that the hiatus may have been originally filled with lens substance which has become absorbed, and Rogman invokes a dislocation of the lens substance within the capsule. The latter idea has been adopted by Kämpffer for cases with insufficiency of the zonule: it merely expresses the same fact in other words.

v. Ammon.—v. Ammon's Zeitschrift, i, 1831. Manz.—In G.-S., ii, 1876. Deutsch-mann.—K. M. f. A., xix, 1881. Höltzke.—A. f. A., xii, 1883. Thalberg.—A. f. A., xiii, 1884. Picqué.—Anomalies de Développement, Paris, 1886. Ginsberg.—C. f. A., xx, 1896. Pflüger.—A. f. A., xiv, 1884. Pfannmüller.—Dissertation, Giessen, 1894. de Wecker. —Traité, iv, 1889. Leber and Addario.—A. f. O., xlviii, 1, 1899. Pichler.—Z. f. A., iii, 1900. E. Fournier.—Thèse de Paris, 1898. Vossius.—A. f. O., xxix, 1, 1883. Deyl. —Anat. Anzeiger, ix, 1896; C. f. A., xxi, 1897. Henckel.—Anat. Hefte, 1898. Chievitz. —Internat. Monatschrift f. Anat. u. Phys., iv, 1887; Anat. Anzeiger, ii, 1888; iii, 1889; Arch. f. mikr. Anat., 1889; Arch. f. Anat. u. Phys., 1890. Lister.—T. O. S., xx, 1900. Lindsay Johnson.—A. f. A., xxi, 1890. v. Ammon.—A. f. O., iv, 1858. van Duyse.—A. d'O., xxi, 1901; Encyclopédie franç., ii, Paris, 1905. Manz.—Internat. Congress, Heidelberg, 1888. Bock.—Die angeb. Colobome des Augapfels, Wien, 1893. Bach.—A. f. O., xlv, 1, 1898. *E. v. Hippel.—In G.-S., 1900; A. f. O., lv, 3, 1903. Salzmann.—xxxix, 4, 1893. *Mannhardt.—A. f. O., xliii, 1, 1897; lx, 3, 1905. Hess.—A. f. A., xli, 1900. Elschnig. —A. f. O., li, 3, 1900. Merkel and Orr.—Anat. Hefte, i, 1892. E. v. Hippel.—A. f. O., xlv, 2, 1898. van Duyse.—A. d'O., xx, 1900. Mitvalsky.—A. f. A., xxv, 1892. Laqueur. —Naturforscher Versammlung, Braunschweig, 1897. Pause.—A. f. O., xxiv, 2, 1878. Cirincione.—Arch. f. Anat. u. Entwicklunsgeschichte, 1897. Plange.—A. f. A., xxi, 1890. Seggel.—K. M. f. A., xxxi, 1893. Hess.—A. f. O., xxxiv, 3, 1888. de Vries.—A. f. O., lvii, 3, 1904. Rumschewitsch.—A. f. O., xxxvii, 4, 1891. Becker.—Zur Anat. d. gesun-den u. kranken Linse, Wiesbaden, 1883. Heyl.—Internat. Congress, 1877; Ann. d'Oc., lxxvii, 1877. Meyer.—B. d. o. G., 1892. Baas.—K. M. f. A., xxxi, 1893. Kämpffer.— A. f. O., xlviii, 3, 1899. Rogman.—A. d'O., xvii, 1897.

Abnormalities of the Vascular System.

Persistent hyaloid artery.—Meissner (1855) first described a strand, 3 mm. long, projecting from the disc of a man's eye as a remnant of the

Fig. 598.—Persistent Hyaloid Artery. Treacher Collins, Researches.

Fig. 599.—Persistent Hyaloid Artery. Treacher Collins, R. L. O. H. Rep., xiii.

hyaloid artery. H. Müller (1856) independently discovered the same strand as a constant feature in the eyes of oxen, undoubtedly the hyaloid artery since it often contains blood in the calf; he foretold that it would soon be observed ophthalmoscopically in man, a conjec-ture which was quickly verified by Saemisch and Zehender (1863). Lawrence (1865) reported the first case in England.

It will be well to recall the anatomy of the normal hyaloid artery. In the fœtus of the third month the central artery of the retina is continued forwards into the vitreous, where it divides dichotomously

into about eight branches and spreads out on the back of the lens to form the posterior vascular sheath. Some of the blood is carried off from the circumlental plexus by veins which enter the cilio-choroidal system, whilst the remainder passes into a peripheral vitreous plexus ultimately to rejoin the central retinal system. The hyaloid artery is not accompanied by any corresponding vein in its course through the middle of the vitreous (Liebreich, 1863), as was held by Richiardi (1869) ; this has been proved by H. Virchow and Schultze.

In the human fœtal eye between the fourth and fifth month the hyaloid artery is surrounded by a distinct cellular sheath, which together with the artery lies in a space lined by a definite hyaline

FIG. 600.—PERSISTENT HYALOID ARTERY.
From the same specimen. Showing the ciliary processes and suspensory ligament.

membrane. Transverse sections in the fifth to sixth months show a hyaline membrane, then a cellular sheath with closely packed cells, then spaces and fibres, and finally the artery in the centre. Farther forward in the vitreous the cellular sheath ceases and the artery lies bare in the canal bounded by hyaline membrane. On approaching the posterior surface of the lens the canal expands, the artery splitting up into branches (Treacher Collins).

By the end of fœtal life the whole of this vitreous-lental system of blood-vessels has become absorbed and has disappeared. In the new-born it is not uncommon to find a tag of the hyaloid artery projecting from the disc (Terrien, $1—1\frac{1}{2}$ mm. long, E. v. Hippel).

The cases in which the artery persists show multitudinous variations. It is usually unilateral (25 bilateral in 174 cases, de Beck).

In most cases the posterior part alone persists for a variable length. In others the whole artery persists, including part of the sheath on the lens, which then forms a so-called posterior polar cataract. In others the central part disappears, both anterior and posterior persisting (Remak, Loring, Hasbrouck, Lawrence); this has been observed in an eye developing myopia, the artery breaking across as the eye elongated (Unterharnscheidt); when only the anterior part persists there is simply a posterior polar cataract, with (v. Ammon, Saemisch, Seely, Webster, Hasbrouck, v. Reuss, Meyer, Kipp) or without a tag behind.

The remnants show either a bluish white, very delicate cord of fibrous tissue, which usually waves about as the eye moves, or such a
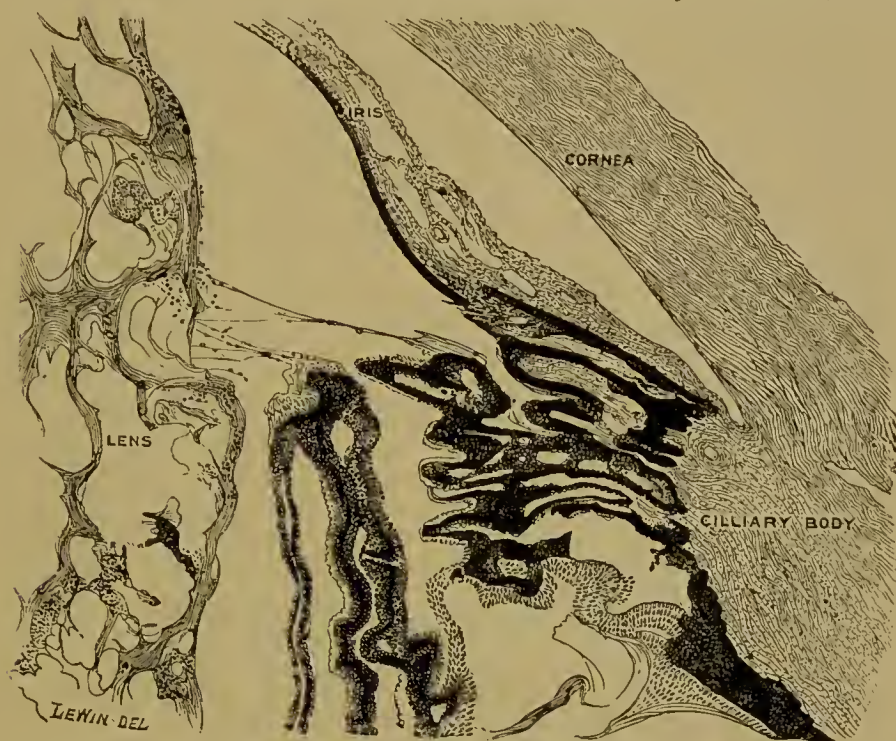
FIG. 601.—PERSISTENT HYALOID ARTERY.
From the same specimen. Showing the suspensory ligament in a more advanced stage of development.

cord is seen to contain a vessel with blood in it, or finally the cord may be thicker and denser, and have new-formed adventitious vessels upon its surface. There is some doubt as to the correct interpretation of these appearances. Thus the first may be attributed rather to persistence of the canal of Cloquet in which the original artery lies than to the artery itself (Manz, de Wecker, Flarer, Schindelka, Galezowski, Despagnet, Holmes, Bayer, Oeller). As opposed to this view the canal of Cloquet is known always to persist, though it is normally invisible ophthalmoscopically; hence there must be some other factor which causes it to become denser and more opaque. Stress has been laid upon this point by Eversbusch, v. Reuss, Magnus, and others. These authors differentiate between the persistent artery and the canal thus: in the former the cord springs from a central vessel on the disc,

its calibre resembles that of this vessel, it passes forwards to the lens, dividing as it goes, and it may be surrounded by a delicate membrane ; in the latter the cord is larger at the disc, and it ends anteriorly in a bulbous swelling or by spreading out into strands or membranes. These characteristics cannot be considered pathognomonic, and Eversbusch lays too much stress upon the importance of myopia as a cause of persistent canal of Cloquet.

Some of the best authenticated variations in appearance may be enumerated. The artery may split up into branches (Gardiner, Bayer, Eversbusch, Tangemann) ; the cord may split into three (Holmes) or more branches ; it may end in a point (Loring), in fine fibrillae (Remak,
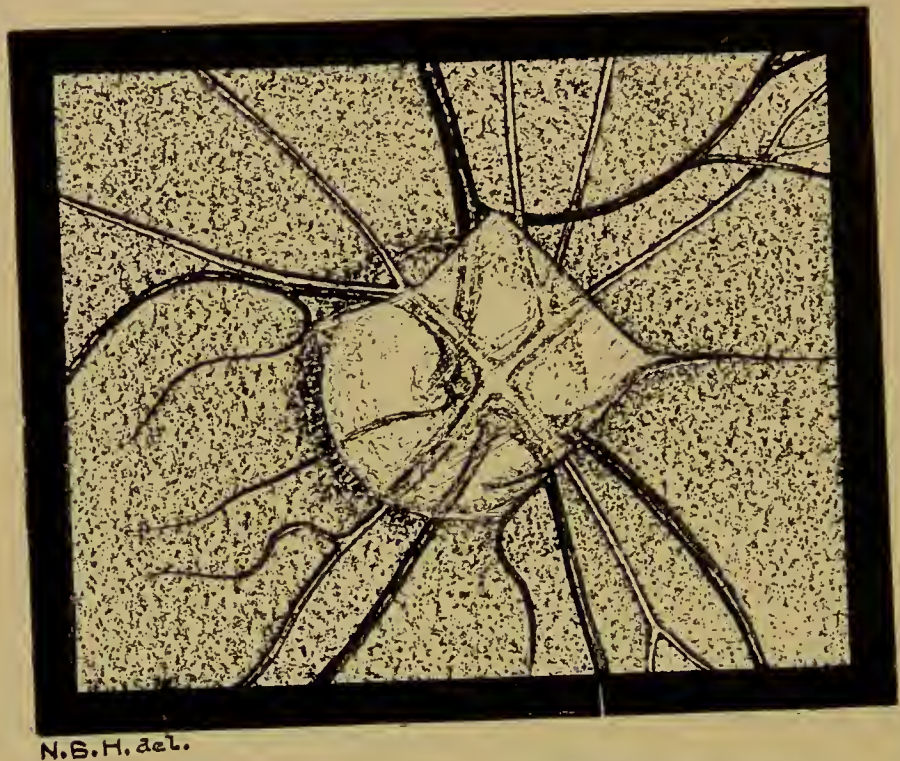
FIG. 602.—PERSISTENT CONNECTIVE TISSUE ON OPTIC DISC.
Harman, T. O. S., xxiii.

van Duyse), in a bulb (de Beck), in grotesque membranes (Wintersteiner, Hirschberg, van Duyse). The mode of insertion both to the disc and to the lens varies. Posteriorly it springs from the central artery or from one of the large branches on the disc, very rarely beyond the disc (e. g. Mooren) or from a macular coloboma (Silcock). The shape is often difficult to make out ; it may be conical, ampulliform, filamentary, or membranous. Very rarely the retina may be pulled up into a small tent-shaped detachment near the disc (Eversbusch, Hersing). When it reaches the lens the insertion is often eccentric—infero-nasal (de Bierre), at the lower edge (Kalcik), infero-temporal (van Duyse). In shape it may be discoid, oval, triangular, or irregular ; by oblique illumination it is greyish white, with or without visible vessels. Opacities in the posterior part of the lens cortex (Otto, Dimmer) are not easily

distinguished from post-capsular ones (Wilde, v. Ammon, Berger, Webster, de Beck); they are usually radial (de Beck).

When there is blood in the persistent artery (Gardiner, Eversbusch, Tangemann, Haab, Hess), pressure on the globe may elicit pulsation: spontaneous "rhythmic movements" have been recorded (Gardiner). There may be blood in a tag which does not reach the lens (Königstein, Kipp, Nettleship).

The following concomitant anomalies have been reported: coloboma of the iris (Wallmann, Eversbusch, Hess); coloboma of the choroid (Goldzieher, de Schweinitz and Randall, Dimmer, Remak, Wallmann, Larsen); macular coloboma (de Beck, van Duyse, Stricker, Silcock); coloboma at the disc (Goldzieher, O. Becker, v. Reuss); cystic
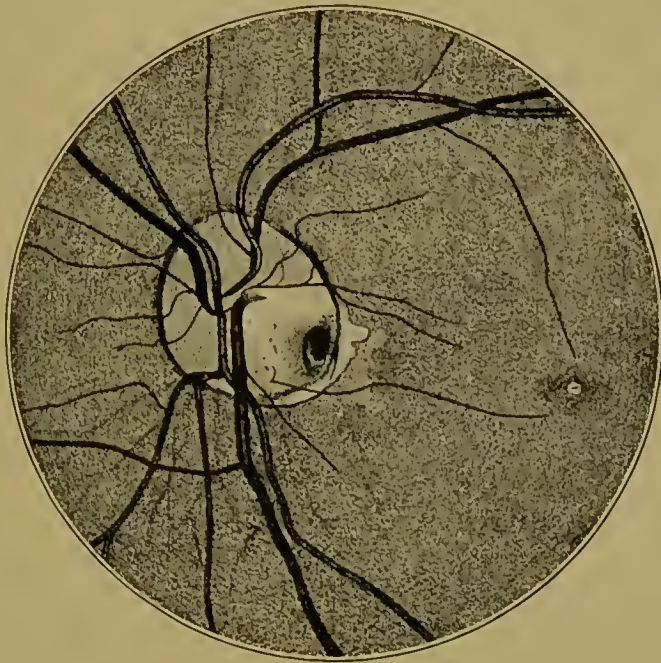
FIG. 603.—HOLE IN THE OPTIC DISC.
Thomson and Ballantyne, T. O. S., xxiii.

coloboma (Wallmann); aniridia (Pflüger, Oeller, Felser, v. Ammon); persistent pupillary membrane (de Bierre, Sulzer, Vassaux, Becker, Flarer); congenital cataract (v. Ammon, Larsen); posterior lenticonus (v. Ammon, Webster, Meyer); anterior lenticonus (Webster); coloboma of the lens (Marcus Gunn); ectopia lentis (Marcus Gunn, de Wecker, Hess); atypical vitreous (Bayer, Sulzer, v. Reuss, Wallmann, Eversbusch); microphthalmia (Becker, Hess); hydrophthalmia (Haab, Berthold); epibulbar dermoids (Badal).

Patches resembling choroiditis are not uncommon in the fundus in these cases (Rockliffe, Randall, Guene, Dimmer, v. Reuss, Hersing, Carter, Lang, Brailey, etc). They have probably different origins in different cases. Some may be regarded as congenital choroiditis (central—Bayer, Holmes), others may be due to hæmorrhage. It is

not improbable that intra-partum hæmorrhage is often the cause, and most of such cases would be diagnosed as truly congenital (*v.* Vol. IV). In some cases there is abnormal pigmentation of the retina (Dimmer, v. Reuss), and this is open to the same two conjectures. Retinitis pigmentosa has been described (Ulrich).

Besides the type of congenital malformation already considered there are allied conditions which are intimately associated with it. Such are deposits of connective tissue on the disc, either in the form of loose ragged masses and strands (Noyes, Hirschberg, Schmidt-Rimpler, Schaumberg, Berger, Ulrich, Little, de Beck) or as delicate, well-defined membranes (Schaumberg, Hirschberg, Fuchs, Loring, Randall, de Beck, Roll (?), Harman) (Fig. 602), and cystic expansions or depres-

FIG. 604.—MICROPHTHALMIA, WITH PERSISTENT HYALOID ARTERY. × 4.
Parsons, T. O. S., xxii. Horizontal section, showing fibrous mass on posterior surface of lens, with anterior end of hyaloid artery, and disc with posterior end of hyaloid artery.

sions on the papilla (Randall, Kollock, Carter, Goldzieher, Holmes, Rockliffe, Königstein, de Beck) (Fig. 603). de Beck considers that the former are remnants of the adventitious tissue around the hyaloid artery, Masselon that they are prolongations from the lamina cribrosa. There can be no doubt that, when congenital, they are remnants of mesoblastic tissue carried in with the central vessels when these become invaginated: this normally disappears almost entirely; in these cases it persists to a greater or less degree.

The delicate veils of membrane stretched across the disc and often passing beyond it show their intimate relation with the vessels by always taking their attachments from them, being stretched between them like a web.

Much larger irregular clumps of connective tissue more or less hiding

Fig. 605.—Microphthalmia, with Persistent Hyaloid Artery   × 18.

From the same specimen. Showing angle of anterior chamber, with fœtal condition of ligamentum pectinatum iridis, and arrest of development of pars plana of ciliary body.
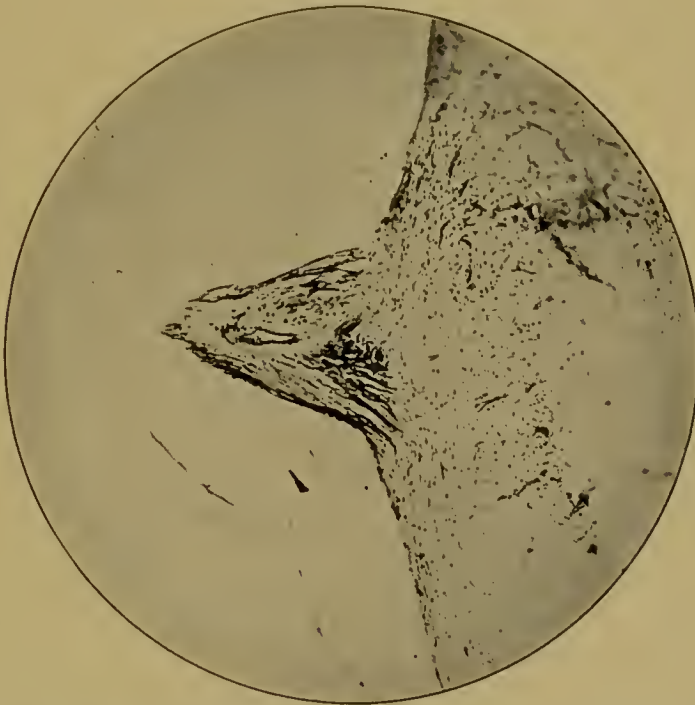
Fig. 606.—Microphthalmia, with Persistent Hyaloid Artery.   × 60.

From the same specimen. Showing vascular fibrous tissue behind lens and anterior end of hyaloid artery.

the disc and often spreading out over a considerable area of the retina are met with (de Schweinitz and Randall, Randall, Guene, Dimmer, Ewetzki, Becker, v. Reuss, Bayer, Brailey, Hersing, Eversbusch, de Bierre, Berger, Saemisch, de Beck, Wintersteiner). Whilst some of these are doubtless congenital and merely exaggerated forms of the commoner shreds and strands, others would seem to be much more reasonably explained as of inflammatory or hæmorrhagic (Mitvalsky) origin. Some have led to confusion with intra-ocular cysticercus ·(v. Graefe, Liebreich, Vassaux).

Cystic expansions or depressions on the disc are rare, judging by the cases reported. They are round or oval, translucent, and pearly grey. Various stages show their origin in persistent hyaloid remains (de
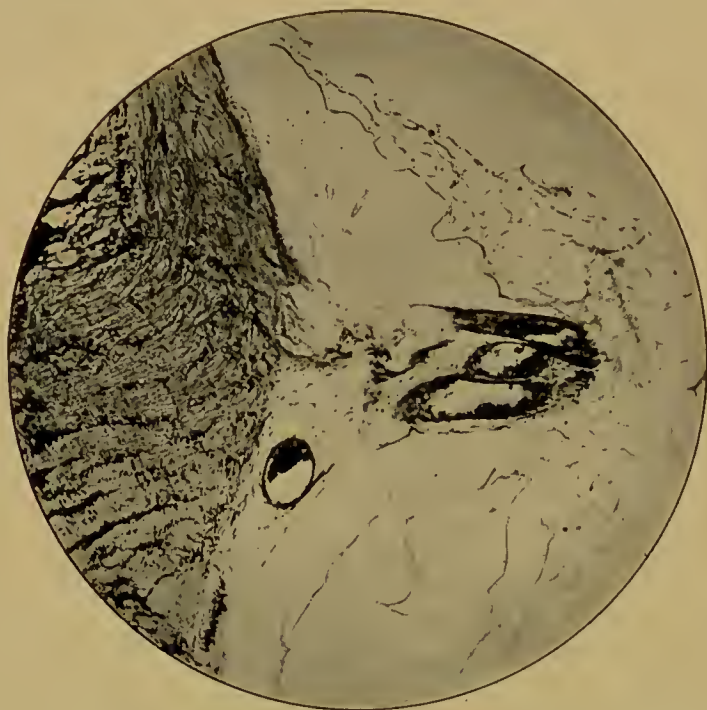
FIG. 607.—MICROPHTHALMIA, WITH PERSISTENT HYALOID ARTERY. × 60.
From the same specimen. Showing optic disc and posterior end of hyaloid artery, which is convoluted, so that it is cut across three times.

Beck). Thus the simplest is a small spherical cyst (Randall, de Beck); then a cyst on a stalk springing from the physiological cup (Kollock, de Beck); then larger round cysts with a knob-like head projecting forwards (Carter, Goldzieher); then flask-shaped cysts (Holmes, Rockliffe); then an ampulliform dilatation containing blood, with a strand stretching forwards into the vitreous (Königstein) or a knob-like expansion at the bifurcation of the central artery (de Beck).

Microscopical examination of the slighter forms of uncomplicated persistent hyaloid artery must necessarily be rare. Most of the cases examined anatomically have been eyes in which the remnants had the clinical features of pseudoglioma, or in which other, more extensive, malformation led to investigation. Manz (1870) reported a case in an anencephalus, and later (1876) one in a girl æt. 24. Nettleship

(1873) described a pseudoglioma in a child æt. 5 : two strands traversed the vitreous; the larger contained two large blood-vessels running the whole length, and taking origin from one or two large retinal vessels at the expanded base; the other cord contained no blood-vessel. They were composed of fibrous tissue containing round or oval cells; the tissue was denser at the outer part. In front the cords expanded and joined a fibrous layer at the back of the lens, and this was continued laterally into the thickened hyaloid covering the ciliary body. Brailey (1876) found a fibrous cord, probably a persistent hyaloid artery, within a detached retina in a boy æt. 15 ; it consisted of fibrous tissue with a denser band in the centre which contained pigment particles. Vassaux (1883) described a persistent hyaloid artery in a child æt. 54 days; it ran from the disc to a deposit on the back of the lens which contained blood-vessels, calcareous particles, and fatty globules. The elongated ciliary processes were fused in the whole circumference with this layer. Partial fusion of the ciliary processes or of duplicatures of the inner layer of the secondary optic vesicle (de Vries) with the posterior vascular sheath of the lens have been recorded several times (Hess, Dötsch, Ginsberg, Treacher Collins, Parsons, de Vries). Three similar cases have been minutely described by Treacher Collins (1890, 1892) (Figs. 599, 600, 601). In one case the artery had its normal coats, contained red corpuscles, and was surrounded by a thick sheath of cells and fibres. The mass on the back of the lens exactly resembled that found in Vassaux' case, and I have had the opportunity of confirming the same features in two cases.

The first case was from a boy æt. 6 months. The eye was cut to one side of the optic nerve. The cornea and a. c. looked normal. A fine strand was seen passing through the vitreous from the optic disc to the centre of the back of the lens. Surrounding it here was a lens-shaped mass of connective tissue, around which was a zone of clear lens at the periphery. Crossing this zone were three ciliary processes, the tips of which were in apposition to the edge of the disc of connective tissue. The other ciliary processes were in their normal situation. The eye was smaller than normal (microphthalmia, antero-posterior diameter = 15 mm.), but showed no other gross abnormalities.

Microscopical examination showed: Cornea and a. c. normal; angles open, do not show undue persistence of spaces of Fontana. Iris stroma more cellular than usual; retinal pigment layer is adherent to lens capsule at pupillary border. The lens with the fibrous mass has the usual bi-convex shape, as the fibrous mass indents the true lens. The anterior capsule and fibres are normal. The anterior epithelium extends rather behind the equator. The posterior capsule is thickened and wavy at the periphery of the fibrous disc ; it is continued in front of this, gradually thinning off towards the posterior pole. There does not appear to be any gap in the capsule. The fibrous mass consists of vascular, densely nucleated connective tissue. Two sets of nuclei stand out distinctly—deeply staining, rod-shaped nuclei, and oval, faintly staining nuclei. The persistent hyaloid artery runs into the mass at the centre behind. There is only a single thin-walled vessel, and this can be traced through the vitreous to the optic nerve. Sections through

the three ciliary processes which meet the fibrous mass show that they are stretched and attenuated. They do not actually join the mass, although they touch it. No vessels can be traced from the mass into them, though it would be impossible to deny that some may be present. Other parts of the eye are normal. There is a ring in the retina near the posterior pole, which may be a rosette, such as is found in glioma and microphthalmia (v. Vol. II, p. 632, Vol. III, p. 827), but is more probably a fold.

The second case was one of a child, æt. 10 weeks, with slight microphthalmia.

Measurements : antero-posterior diameter = 15·5 mm. ; transverse = 15·5 mm. ; vertical = 15·5 mm. There was no gross abnormality other than the general diminution in size.

Macroscopic examination showed cornea normal ; a. c. good, 2 mm. deep ; angles apparently open. Iris normal ; pupil small ; lens looks normal in front ; the ciliary processes are in contact with it rather in front of the equator. Vitreous full of flocculent white material ; one slightly more definite strand passes forward from the optic disc to a mass of denser tissue on the back of the lens. The flocculent matter is equally distributed throughout the vitreous. Retina and choroid in situ ; both apparently normal, the former being relatively thicker than in the adult condition. There is no evidence of incomplete closure of the fœtal cleft.

Microscopic examination showed cornea normal ; a. c. good ; angles open. The angles are interesting as showing the typical fœtal condi-tion—i. e. a true ligamentum pectinatum iridis, with well-developed spaces of Fontana, as in lower animals (Fig. 605). The canal of Schlemm is large, widely open, and empty. Iris and ciliary body normal. The ciliary processes are long and thin, and nearly touch the lens at or in front of the equator. Fibres stretch from them to the lens and into the mass of tissue behind the lens. There are nuclei to be seen upon some of them. Lens : anterior capsule normal ; the cubical cells are continued round the equator, and line the peripheral parts of the posterior capsule ; the central parts of the posterior capsule are wavy, and apparently broken up by the tissue which covers the posterior sur-face ; the peripheral parts of the posterior capsule are thickened, and very wavy upon one side, as if retracted. The cortex of the lens is maldeveloped, showing swollen, nucleated cells and fibres, arranged irregularly. The nucleus is homogeneous, containing some aggregations of small cells with deeply-stained nuclei. Behind the lens, and in apposition to it, is a lens-shaped mass of very dense and cellular con-nective tissue, extremely richly supplied with blood-vessels (Figs. 604, 606). It projects in the centre posteriorly into a pyramid, which con-tains the patent hyaloid artery. The vitreous is full of a loose meshwork of non-nucleated fibres, which stain with eosin, are wavy, and irregular in width. They are most marked at the peripheral parts, near the surface of the retina. A few pigment-cells, free pigment-granules, and one or two clumps of small nucleated cells are to be seen in the network. Optic disc : there is an apical projection, placed somewhat eccentrically upon the surface of the disc. It contains the hyaloid artery cut

obliquely. It is patent and contains blood-corpuscles. In some sections there are apparently three vessels lying side by side, an appearance probably due to a double twist in the hyaloid artery (Fig. 607). In other sections a single vessel is seen, cut obliquely in two places, one nearer the disc, the other nearer the lens. There is therefore probably only a single vessel present, and this can be traced throughout the length of the vitreous in the series of sections. Retina looks quite normal except in the pars ciliaris, where it shows arrested development. On one side it ends abruptly behind a ciliary process, passing immediately into the non-pigmented layer of cells. On the other it ends in a fold, showing small cystic spaces in the inner nuclear and the nerve-fibre layers. The apex of the fold is tied down to the tissue behind the lens, and is in
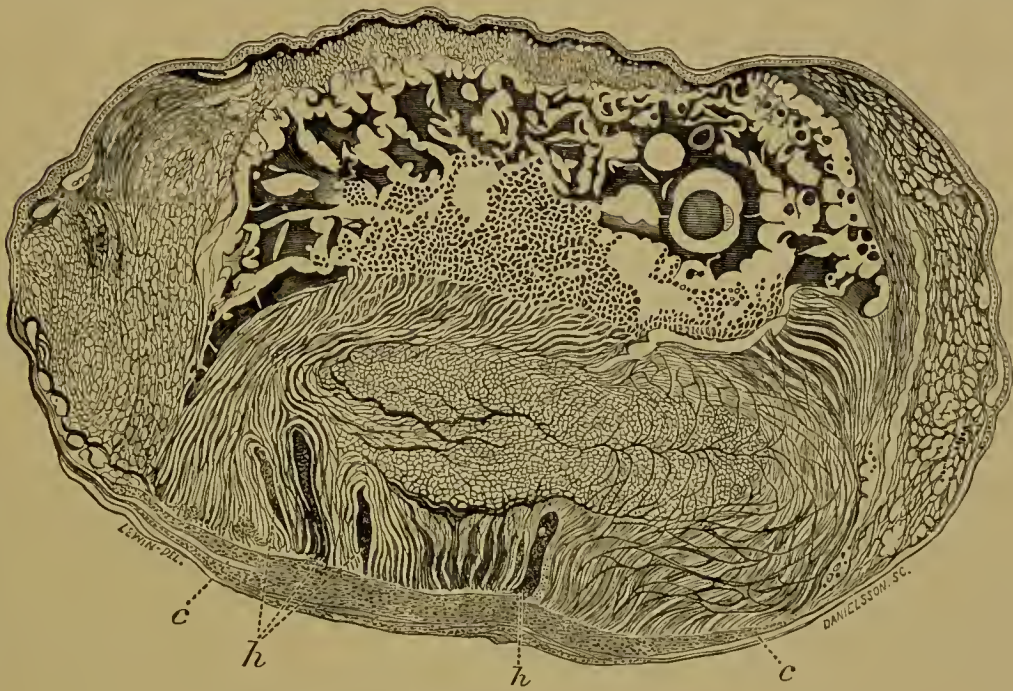
FIG. 608.—PERSISTENT POSTERIOR SHEATH OF LENS.
Treacher Collins, R. L. O. H., xiii. The lens is cataractous. *c, c.* Ends of posterior capsule, the space being occupied by vascular connective tissue. *h, h.* Hæmorrhages in lens substance.

direct contact with it. There is no projection of the retina at the disc, but small cystic spaces at this part are evidence of some traction. Optic nerve normal. Sclera is rather disproportionately thick.

Allied cases are those of persistent posterior vascular sheath of the lens—so-called posterior polar cataract—without any remnants of the hyaloid artery. Treacher Collins and I have each described one such case. In the former's there was hæmorrhage into the lens, so that the hyaloid artery cannot have been long atrophied (Fig. 608). In mine, from a child aged 4 months, the cornea was normal, anterior chamber shallow, angles open, canal of Schlemm patent, iris normal, lens fibres and anterior capsule normal. The posterior capsule was replaced by a layer of fibro-cellular tissue, which was continuous with similar tissue forming the suspensory ligament, and with delicate

fibres running through the vitreous. The capsule behind the equator of the lens was much thickened, and was wavy posteriorly, where it dwindled away and disappeared in the cellular tissue. In sections near the periphery of the lens it was seen that the lens-fibres overlapped the irregular margin of the gap in the capsule, and here the fibro-cellular tissue was much thicker. The ciliary processes were in contact with the edge of the lens ; they showed no signs of inflammation. The retina and choroid were normal. The optic nerve was normal, and there was no trace of a persistent hyaloid artery.

In Treacher Collins's case there was also no hyaloid artery, although there was hæmorrhage into the lens. The similarity in the nature of the tissue has been confirmed by actual comparison of sections under the microscope. It is open to regard the tissue as newly formed, the result of inflammation. Opposed to this view are the following considerations : (1) the dissimilarity of the fibro-cellular tissue to newly-formed inflammatory tissue ; (2) the absence of inflammatory deposits in other parts of the eye ; (3) the shallow anterior chamber ; (4) the contact of the ciliary processes with the lens, pointing to arrest in development : (5) the dense mass of nucleated fibres in the position of the suspensory ligament.

MEISSNER.—Z. f. rat. Med., i, 1855.   H. MÜLLER.—Würzburger Verhandlungen, 1856 ; A. f. O., ii, 2, 1856 ; Gesammelte Schriften, i, Leipzig, 1872.   SAEMISCH, ZEHENDER.—K. M. f. A., i, 1863.   LAURENCE.—Ophth. Rev., 1865.   LIEBREICH.—K. M. f. A.. i, 1863. RICHIARDI.—In Nagel's Jahresbericht, 1871.   H. VIRCHOW.—Phys. med. Gesellschaft zu Würzburg, 1879.   O. SCHULTZE.—v. Kölliker's Festschrift, 1892.   TREACHER COLLINS.— Researches, London, 1896.   TERRIEN.—A. d'O., xvii, 1897.   E. v. HIPPEL.—A. f. O., xlv, 2, 1898.   *DE BECK.—Persistent Hyaloid Artery, Cincinnati, 1890.   REMAK.—C. f. A., ix, 1885.   LORING.—Textbook of Ophthalmoscopy, New York, 1886.   HASBROUCK.—Jl. of O., i, 1889.   UNTERHARNSCHEIDT.—K. M. f. A., xxx, 1892.   v. AMMON.—Klin. Darstellungen, Berlin, 1847.   SAEMISCH.—K. M. f. A., vii, 1869.   SEELY.—T. Am. O. S., 1882.   WEBSTER. —A. of O., iv, 1874.   v. REUSS.—Mitth. d. II Wiener Klinik, ii, 1885.   MEYER.—C. f. A., xii, 1888.   MANZ.—In G.-S., ii, 1876.   DE WECKER.—K. M. f. A., vii, 1869.   FLARER.—In Nagel's Jahresbericht, 1870.   SCHINDELKA.—Wiener med. Blätter, vii, 1884.   GALEZOWSKI. —Rec. d'O., 1882.   DESPAGNET.—Soc. franç. d'O., 1888.   BAYER.—Prager Z. f. Heilkunde, iv, 1883.   OELLER.—Dissertation, München, 1878.   EVERSBUSCH.—Mitth. a. d. Klinik München, 1882.   MAGNUS.—K. M. f. A., xxv, 1887.   GARDINER.—A. of O., ix, 1880. TANGEMANN.—A. of O., xvii, 1888.   WINTERSTEINER.—A. f. A., xxviii, 1894.   HIRSCHBERG. —Einführung in d. Augenhkde., ii, Leipzig, 1901.   MOOREN.—Ophthalmiatrische Beobach-tungen, Berlin, 1867.   SILCOCK.—T. O. S., xv, 1895 ; xx, 1900.   HERSING.—K. M. f. A., xxii, 1884.   DE BIERRE.—Soc. d'O., 1886.   KALCIK.—Wiener med. Woch., 1897.   *OTTO. —B. z. A., v, 1892.   DIMMER.—A. f. A., xiv, 1884.   WILDE.—An Essay on Malformations, London, 1862.   BERGER.—K. M. f. A., xxii, 1884.   HAAB.—A. f. O., xxiv, 2, 1878.   HESS. —A. f. O., xxxiv, 3, 1888.   KÖNIGSTEIN.—Wiener med. Woch., 1884.   NETTLESHIP.— R. L. O. H. Rep., vii, 1873.   WALLMANN.—Z. d. Gesellschaft d. Aerzte zu Wien, 1858. STRICKER.—A. of O., xxiii, 1894.   DE SCHWEINITZ AND RANDALL.—A. of O., xvii, 1888. FELSER, SULZER.—K. M. f. A., xxvi, 1888.   VASSAUX.—A. d'O., iii, 1883.   MARCUS GUNN. —T. O. S., ix, 1889.   BERTHOLD.—A. f. O., xvii, 1, 1871 ; Klin. Darstellungen, iii, 1882. ROCKLIFFE.—T. O. S., vii, 1887.   RANDALL.—T. Am. O. S., 1888.   CARTER.—T. O. S., vi, 1886.   LANG.—T. O. S., v, 1885.   BRAILEY.—R. L. O. H. Rep., viii, 1876.   DÖTSCH, GINSBERG.—A. f. O., xlviii, 1, 1899.   ULRICH.—K. M. f. A., xx, 1882.   NOYES.—Internat. Congress, New York, 1877.   SCHMIDT-RIMPLER.—A. f. O., xxiii, 4, 1877.   SCHAUMBERG.— Dissertation, Marburg, 1882.   LITTLE.—T. Am. O. S., 1882.   FUCHS.—A. f. O., xxviii, 1, 1882.   ROLL.—T. O. S., xxii, 1902.   HARMAN.—T. O. S., xxiii, 1903.   MASSELON.—In de Wecker and Masselon, Manuel d'O., 1889.   MITVALSKY.—A. f. A., xxviii, 1894.   TREACHER COLLINS.—R. L. O. H. Rep., xiii, 1, 1890 ; xiii, 3, 1892.   PARSONS.—T. O. S., xxii, 1902 ; xxiii, 1903.   SALFFNER.—A. f. O., liv, 3, 1902 (Bulbus septatus).   POLTE.—Z. f. A., xi, 1903. DE VRIES.—A. f. O., lvii, 3, 1904.   *VAN DUYSE.—A. d'O., xi, 1891 ; Encyclopédie franç., ii, Paris, 1905.

Persistent vessels in the vitreous (other than the hyaloid artery). —Hirschberg (1883) described bunches of fine vessels in the periphery of the vitreous, springing from the retinal vessels near the disc as persistent fœtal vessels. Wintersteiner supports this view. Such vessels, sometimes resembling the pecten of birds, must be regarded as new-formed vessels, and rarely, if ever, congenital. They are most common in syphilitic cases, but also occur after vitreous hæmorrhages (retinitis proliferans, q.v.). The peripheral fœtal vitreous vessels are all veins, and disappear early, whilst the presence of a hyaloid vein is unknown.

Congenital vascular loops springing from veins are exceptional (Frost, Szili Jnr., Hirschberg, Coats). They usually arise on the disc
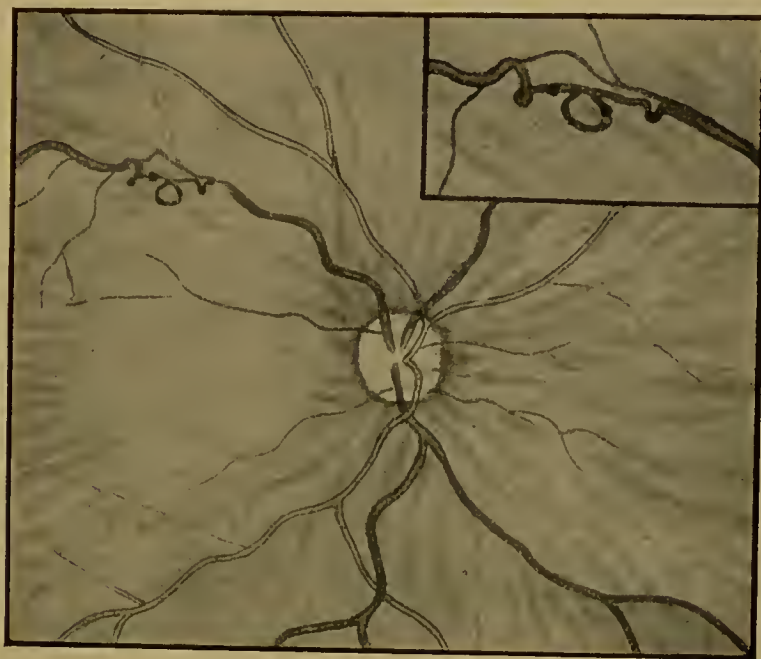
FIG. 609.—RETINAL VENOUS LOOP.
Coats, T. O. S., xxv.

and fall back to the fundus close to the point from which they originated. The case described by Coats, if it is to be considered congenital, is an exception, since it occurred at some distance from the disc and much resembled a newly-formed anastomosis.

HIRSCHBERG.—C. f. A., vii, 1883; xiv, 1890; Einführung, Leipzig, 1901. STORY.— T. O. S., iii, 1883. NETTLESHIP.—T O. S., iv, 1884. FROST.—T. O. S., vii, 1887; Atlas, Plate XXI, fig. 25, 1896. WINTERSTEINER, MITVALSKY.—A. f. A., xxviii, 1894. GLOOR.— A. f. A., xxxv, 1897. SZILI JNR.—Augenspiegelstudien, Pl. I, Wiesbaden, 1901. COATS.— T. O. S., xxv, 1905.

Prepapillary retinal arteries.—An arterial coil, passing forwards for a short distance into the vitreous, has been observed by Czermak (1883), Hirschberg, Frost, Wachtler, Bondi, Günsburg, and Hirsch. The recurrent vessel is not a vein, though it may pass into the disc close to and under a vein (Hirschberg). In a remarkable case of Hirschberg's the vessel passed into the vitreous, then broke up into

numerous branches, which curved round and entered the peripheral part of the retina.

These abnormal arteries have been considered persistent hyaloid arteries. They show very little resemblance to these in their usual form; neither are they new vessels of inflammatory origin, for undoubted cases of this type are also quite different in appearance. Czermak and Hirschberg consider that they are persistent vitreous vessels, but these are veins. In the present state of knowledge of the development of the retinal vessels it is impossible to give a satisfactory view of their origin.

Czermak.—C. f. A., vii, 1883. Hirschberg.—C. f. A., ix, 1885; Einführung, ii, Leipzig, 1901. Frost.—T. O. S., vii, 1887. Wachtler.—Wiener med. Woch., 1896. Bondi, Günsburg, Hirsch.—K. M. f. A., xxxvii, 1899.

Tortuosity of the retinal vessels.—The retinal vessels are sometimes extremely tortuous, either in one eye only (Horrocks, Levin, Work Dodd, Hartridge) or both (Benson, Nettleship, Stephen Mackenzie, Pick), and involving both arteries and veins, or veins only (Magnus, Nettleship, Horrocks, Stephen Mackenzie, Hartridge). The condition is usually associated with hypermetropia (*e. g.* Benson, Nettleship, Stephen Mackenzie) or with angioid conditions of the skin of the face and other parts of the body (Horrocks, Work Dodd, Hartridge).

The association with hypermetropia may be ascribed to a normal growth of the vessels, with insufficient expansion of the globe, but, as mentioned, the veins alone are most frequently affected; the retina is not folded. When associated with angiomata, which are always capillary, there is no anastomosis of the vessels. One of Stephen Mackenzie's cases had emphysema.

Magnus.—Atlas, Breslau, 1872. Benson, Nettleship.—T. O. S., ii, 1882. Horrocks. —T. O. S., iii, 1883. Stephen Mackenzie.—T. O. S., iii, 1883; iv, 1884. Levin.—A. f. A., xxxviii, 1899. Pick.—A. f. A., xxxix, 1899. Work Dodd, Hartridge.—T. O. S., xxi, 1901.

Absence of retinal vessels.—v. Graefe observed complete absence of the retinal vessels in the well-developed blind eye of a boy æt. 10. This was ascribed to arrested development by H. Müller. Retze has described congenital absence of retinal vessels and papilla nervi optici in the somewhat microphthalmic eye of a girl æt. 4. These cases are held by some to be analogous to the absence of the canal of Schlemm in buphthalmia (q.v.).

v. Graefe.—A. f. O., i, 1, 1854. H. Müller.—Gesammelte Schriften, Leipzig, 1872. Retze.—B. z. A., xlvii.

Arterio=venous anastomosis.—This has been observed by Marcus Gunn, but is excessively rare. In such cases no varicose condition of the vein occurs, probably owing to the support afforded by the intra-ocular tension.

Marcus Gunn.—T. O. S., iv, 1884.

Bifurcation of the veins.—This has been observed several times

occurring on the disc. The branches often also communicate with other veins.

FROST.—T. O. S., ix, 1899. WERNER.—T. O. S., x, 1890. STEPHENSON.—T. O. S., xi, 1891.

Cilio-retinal and optico-ciliary vessels.—These vessels, the distribution of which is evident from their names, should be carefully distinguished, since the former are common and the latter rare.

Cilio-retinal arteries are quite common; they were first discovered by Donders and H. Müller, and demonstrated anatomically by Nettleship. They are always situated on the temporal side of the disc, and pass to the macular area (Nettleship). Typically they appear at the edge of the disc, pass in towards the centre, then bend sharply outwards to pass into the retina. If they have not this characteristic bend it is impossible to be certain that they are not branches of the central artery before it comes to the surface. Accepting this criterion, Lang and Barrett found 8—16·7 per cent. of undoubted cases in a large number of Moorfields patients, 3—6·3 per cent. of doubtful cases. They are generally unilateral. Nettleship proved in one case that the artery was a scleral vessel, not choroidal; unfortunately, the case was one of choked disc, so that the vessel might be interpreted as one of new formation. The observation has, however, received ample confirmation (Elschnig).

Czermak divides cilio-retinal arteries into four groups: (1) the ordinary type, ending at the choroidal border of the disc; (2) the vessel disappears into the sclera—*e. g.* in the conus, without showing any relation with any retinal or choroidal artery; (3) the vessel springs fruo a sclero-choroidal vessel; (4) the artery springs from a choroidal vessel. The fourth group is not proved. Elschnig has controlled the existence of the other groups by anatomical demonstration: (1) a branch of the circle of Zinn (*v.* Chap. XVII) perforates the sclerotic obliquely without communicating with the choroid in the intra-scleral or intra-choroidal portion of the disc; (2) the branch, springing from the arterial circle, passes between the choroid and the disc or enters the choroid; it divides into two or more branches, one of which becomes a cilio-retinal vessel, whilst the others pass into the choroid; (3) the cilio-retinal vessel springs from a choroidal vessel, but this is itself a branch of the arterial circle, not an ordinary posterior ciliary. From the examination of eleven cases, Elschnig proved that all cilio-retinal arteries are branches of the circle of Zinn, as already held by Leber.

Cilio-retinal arteries are terminal arteries, as shown by cases of embolism of the central artery (*e. g.* Hirsch).

Cilio-retinal veins are much rarer than the arteries (*cf.* Kuhnt), probably owing to the almost total absence of veins in the circle of Zinn (Leber). When observed they are probably of new formation, following inflammation.

Optico-ciliary vessels are very rare; 8 indubitable cases have been reported (Braune), 7 being veins (Elschnig, Rumschewitsch, Nickels, Niels Höeg, Braune), and 1 an artery (Oeller); another case of optico-ciliary vein has been recorded by Lawford, and another artery by Benson

(1883). They are twigs of the central retinal vessels which do not pass into the retina, but disappear into the choroid under the edge of the disc. All the cases have been unilateral. Other cases have been described under this category, but were probably of new formation (Vossius, post-neuritic atrophy; Elschnig, glaucoma, tumour; Salzmann, tumour). The veins are sometimes of the same tint as the other central veins, sometimes much paler, the difference being due to their depth (Elschnig). The veins are often much broader than the normal veins. Elschnig and Niels Höeg regard their cases as so-called posterior vortex veins (*v. infra*).

DONDERS.—A. f. O., i, 1855. H. MÜLLER.—Z. f. wissensch. Zool., viii, 1856. NETTLE-SHIP.—R. L. O. H. Rep., ix, 1877. MAUTHNER.—Lehrbuch d. Ophthalmoscopie, 1868.

FIG. 610.   FIG. 611.
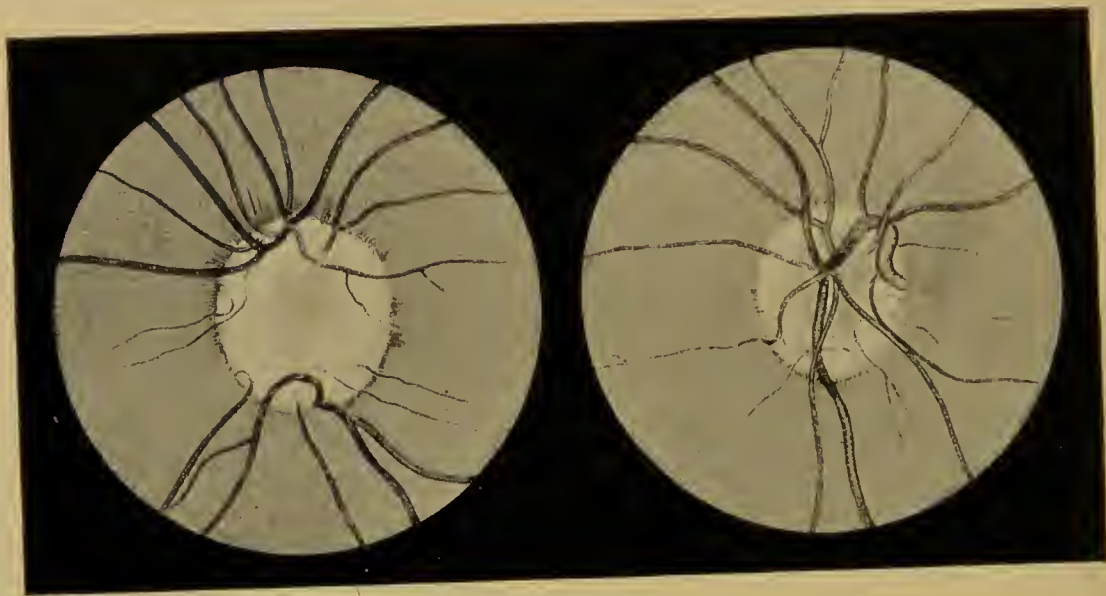
FIGS. 610 AND 611.—ABNORMAL RETINAL VESSELS.
Lawford, T. O. S., xv. Fig. 610, left eye, all the vessels emerging from the margin of the disc. Fig. 611, right eye, with large optico-ciliary vein.

LORING.—C. f. A., ii, 1877. SCHLEICH.—Mittheilungen, Tübingen, 1880. CZERMAK.—Wiener klin. Woch., 1888. LANG AND BARRETT.—R. L. O. H. Rep., xii, 1888. ELSCHNIG.—A. f. O., xliv, 1, 1897. LEBER.—In G.-S., ii, 1876. HIRSCH.—A. f. A., xxxiii, Ergänzungs-heft, 1896. KUHNT.—B. d. o. G., 1881. BENSON.—T. O. S., iii, 1883. ELSCHNIG.—A. f. A., xviii, 1888; K. M. f. A., xxxvi, 1898. RUMSCHEWITSCH, NICKELS.—K. M. f. A., xxvii, 1889. NIELS HÖEG.—A. f. O., lv, 2, 1903. *BRAUNE.—K. M. f. A., xliii, 1905. LAWFORD.—T. O. S., xv, 1895. OELLER.—Atlas seltener ophthalmosc. Befunde, 1904. SALZMANN.—A. f. O., xxxix, 4, 1893.

Choroido-vaginal veins (" Posterior vortex veins ").—The occurrence in highly myopic eyes of large venous trunks, which closely resemble vortex veins but disappear in the neighbourhood of the disc, has only recently aroused the attention of ophthalmologists. They are pictured though not described by Liebreich in his ' Atlas,' and again by Czermak, who spoke of them as " abnormal vortex veins." The first clear recognition and account of them, however, is due to Schoute (1898). Referring to this paper in Nagel's ' Jahresbericht ' of the same year,

Axenfeld expressed the opinion that although previously undescribed, they were not of very infrequent occurrence. In 1903 Schoute was able to refer to 13 cases of his own and 2 by van der Hoeve. Pictures of the condition will be found in the ' Atlases' of Oeller and Haab; that given by Oeller is the most typical.

In all these cases, except one of Schoute's, the eyes were myopic, and in some the myopia was certainly progressive; in the exception there was slight hypermetropia. Thomson and Ballantyne have reported two other cases in hypermetropes, together with a case in a myope. They state that they have " each seen several cases in which a larger or smaller number of veins in one or both eyes converged towards the sheaths of the optic nerves."

Coats considers that they are uncommon but not extremely rare if one watches specially for them, but they are easily overlooked or wrongly interpreted. They occur as large, sometimes enormous, vessels, without lustre or reflex, and lying behind the retinal vessels. In Oeller's case the largest of them measured half the diameter of the disc. They collect blood from a ramified system of broad trunks, often extending over a large area of the fundus, very much in the same manner as a true vortex vein; so that the term " posterior vortex vein " is clinically very apt. The large trunk formed by the junction of these ramifications disappears at or near the edge of the disc, or within a myopic crescent, or at its outer edge. They are not confined to one or other side of the disc, but are probably seen most frequently downwards and outwards. That they are veins and not arteries has been proved, if proof were necessary, by observing that on applying pressure to the globe the central end empties while the branches remain normally filled, or possibly become fuller and darker.

The condition is not to be confounded with mere visibility of the choroidal vessels due to thinning and atrophy of the choroid. In normal circumstances the choroidal blood even from the neighbourhood of the papilla is collected by the equatorial vortex veins, the minute branches which enter the nerve from the choroid being too small to be visible ophthalmoscopically. The course of the blood towards the disc and the disappearance of these huge trunks at its edge constitute something quite abnormal and very striking when attention has been called to it. Moreover, they are only seen with great rarity in poorly pigmented emmetropic or hypermetropic, or in albinotic fundi. So large and dull-coloured are they that in many cases they have been mistaken for hæmorrhages. In the first case reported by Schoute the vein had been seen thirteen years before, but had been recorded in the notes as an extravasation of blood.

Up to the present practically nothing has been done from the pathological standpoint to elucidate these appearances. There is no exact knowledge as to what becomes of the veins after their disappearance, and into what vessels their blood is poured. Moreover there have been few suggestions as to why they should occur, and why they should be so frequently found in highly myopic eyes. It has been supposed that they are simply congenital abnormalities. The vortex veins are notoriously inconstant in number and position, and it has

been suggested that in the cases under consideration one is merely abnormally inserted in the neighbourhood of the nerve. But this does not take account of their frequency in high myopia, and is not a probable explanation of cases in which there are several such veins (five in a case of Haab's and in two of Thomson and Ballantyne's cases). It receives a certain amount of support, however, from a case reported by Axenfeld and Yamashita in which a large vessel, resembling in form and size a vortex vein, pierced the sclerotic from the choroid close to the nerve on the temporal side. This had not been seen ophthalmoscopically and occurred in an emmetropic eye. It was discovered accidentally in the microscopical preparation. In com-

FIG. 612.—CHOROIDO-VAGINAL VEIN.   × 30.
Coats, Ophth. Rev., xxv.   A. Junction of dural sheath (D) of the nerve with the sclerotic.   I. Anterior part of intervaginal space.   B. Scleral promontory.   P. Pial sheath of optic nerve.   V. Choroido-vaginal vein.

menting upon this Axenfeld and Yamashita raise the question whether such veins may not occur as a congenital abnormality with equal frequency in hypermetropic, emmetropic, and myopic eyes, but only become visible in highly myopic eyes in consequence of choroidal thinning. But here again the explanation is improbable where there are several veins, and it does not take account of the frequency with which they disappear at or very close to the edge of the disc.

A step in advance was taken by van Geuns, who pointed out that the vessels concerned are probably the same as those which give rise to optico-ciliary veins (q. v.), i.e. the occurrence on the disc of a large branch of the central vein, which disappears at its edge into the choroid (as has been proved anatomically by Elschnig). van Geuns,

following Elschnig, believes that such veins represent a congenital enlargement of the normal minute anastomoses between the choroidal and central vessels on the nerve-head, and suggests that choroido-vaginal veins differ from them only in degree. Optico-ciliary veins disappear on reaching the periphery of the disc because they are hidden in their further course by the retinal pigment ; choroido-vaginal veins, which are visible in the fundus in myopic eyes on account of the choroidal thinning, disappear on reaching the disc because they lie deeper in the nerve than the visible optico-ciliary veins. The connection between the two is furnished by a case of Elschnig's, where an optico-ciliary vessel was visible for some little distance beyond the edge of the disc in consequence of poor pigmentation of the fundus, and
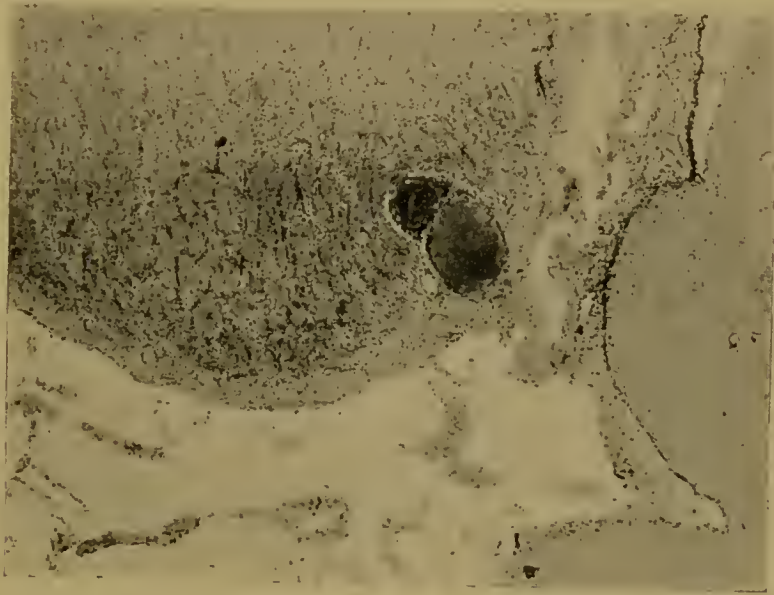
FIG. 613.—CHOROIDO-VAGINAL VEIN. × 30.
From the same specimen. Junction of a trabecular vein with the choroido-vaginal vein. Note situation close under the pial sheath.

presented a certain resemblance to a choroido-vaginal vein. Coats has described the anatomy of a choroido-vaginal vein in a myopic eye.

The abnormal vein was found on the nasal side, and its relations can best be followed by studying Fig. 612. (A) shows the point where the dural sheath of the nerve (D) joins the sclerotic. It therefore marks the anterior end of the intervaginal space (I), and may be taken as a useful landmark from which to orient. (B) is the point from which the lamina cribrosa springs, and shows also the place where the choroid and retina end. The wide area between (A) and (B) therefore corresponds to the very small area in the normal eye, which lies over the anterior end of the intervaginal space, and within that point. This shows the great elongation which the scleral promontory, and with it the choroid and retina, have undergone. (P) is the pial sheath of the nerve, which is also inserted into the ending of the sclera. (V) is an extremely large vessel which emerges from the choroid within the elongated area, and piercing the tissues of the scleral promontory

obliquely near its end runs up the nerve close to and within the pial sheath. The vessel is a typical vein, with a well-marked endothelial lining, but no muscular fibres in its wall; it is filled with blood. Following it farther up the nerve, it makes one or two sharp bends, but remains always close under the pial sheath. It is certainly much larger than the central vein, and is probably even larger than would appear from the photograph, since it is found in a considerable number of sections. This would correspond to the usual ribbon-like appearance of these vessels. Some distance up the nerve it is joined by another branch about half its size from the supporting trabeculæ. Unfortunately, the series of sections is not complete enough to say exactly whence this vessel comes, so that one cannot be sure whether it is another similar branch from the choroid or an offshot from the central vein. The latter is perhaps more probable, as it lies well within the nerve-substance and nearer the central vessels, more peripherally. The piece of nerve excised with the globe does not extend far beyond the point of junction of the two veins, so that the final termination of the vessel formed by them is unknown, but so far as the sections go it does not leave its position close to the pial sheath. A normal central artery and vein are present in the usual position.

It is unfortunate that the fundus could not be observed ophthalmo-scopically in this case, so that the final link of a choroido-vaginal vein, observed both clinically and microscopically, must still await future research. But there can be hardly a doubt that this huge choroidal vein, plunging into the deeper tissues in close proximity to the papilla, must, if visible at all, have presented the appearance of a choroido-vaginal vein. It will be noted that its course confirms the supposition of Oeller and van Geuns that these veins must pass backwards by one of the sheaths of the nerve.

The explanation of van Geuns, that choroido-vaginal veins arise from an unusual development of the normal anastomoses round the nerve entrance, seems by far the best (Coats). The supposition that they are merely abnormally placed vortex veins might be feasible if they ran outside or even within the dural sheath, but is highly impro-bable when they are found to lie within the pia. Moreover, as already pointed out, the theory of abnormal vortex veins becomes very unlikely when there are more veins than one. Van Geuns's hypothesis has also the advantage of deriving them from structures already present normally, instead of supposing new and abnormal formations.

According to Leber, the anastomoses between twigs of the choroidal and central vessels around the nerve-entrance are in three directions: (1) backwards to the pial sheath; (2) straight inwards to the region of the lamina cribrosa; (3) forwards to the papilla to take part in its vascularisation. It seems that each of these is capable of congenital or pathological enlargement. The first is evidently the anastomosis involved in the cases now under consideration, as is shown by the anatomical relations of the abnormal vein, which remains close to the pial sheath during the whole of its course, and is connected (probably) with the central vein, not directly, but through a greatly enlarged trabecular branch. In both of these points it corresponds with the

normal vessels of the pial sheath. The second anastomosis when enlarged gives rise to optico-ciliary veins, as has been proved anatomically by Elschnig. It would appear, therefore, that the difference between choroido-vaginal and optico-ciliary veins is not merely one of degree, as van Geuns has stated, but that a different anastomosis is involved. The third anastomosis probably gives rise to the little nets and bunches of tortuous vessels sometimes seen at the edge of the papilla in cases of obstruction of the central vein or its branches. It should be noted that none of these anastomoses has anything to do with the circle of Zinn, which is a purely arterial circle belonging to the scleral part of the nerve-entrance and with no corresponding venous twigs.

Choroido-vaginal veins have always been regarded as congenital abnormalities; indeed, Oeller considers their presence a proof that any associated crescent is also congenital. Although a probable connection with the anastomoses about the nerve-head has been pointed out, it has been considered that this connection was merely in the form of a congenital enlargement of these anastomoses. This, however, does not take account of their frequent association with high myopia. It has, indeed, been suggested that they are not more frequent in myopia, but only more frequently visible owing to choroidal thinning. If, however, such enormous veins passed from the choroid into the pial sheath with any degree of frequency, they could not have failed to be observed microscopically and reported. There can be little doubt that there is a definite connection between their occurrence and high myopia. Coats suggests that the connection is one of cause and effect. In the myopic globe the yielding and expansion of the tunics chiefly or entirely affects the posterior hemisphere. The vortex veins are therefore practically left in their normal positions, while the posterior pole of the eye is removed a long distance from them. This must constitute a certain hindrance to the return of the venous blood, which normally flows from the posterior pole to the equatorial vortex veins. But, in addition, the choroid, as is well known, undergoes much thinning and atrophy in consequence of the stretching to which it is subjected, and this must add considerably to the difficulty which the venous blood encounters in finding its way by the normal channels from the region about the nerve entrance. Especially will this be so on the temporal side of the disc, because it is on this side that the giving way of the tunics is always most pronounced in myopic eyes. Under these circumstances the blood from the posterior pole of the eye, meeting with obstruction to its normal outflow, will seek out any anastomotic channels which it can find, and these are already provided at the nerve-entrance. The enormous size of these veins in some cases need cause no astonishment when it is remembered over how long a period the conditions giving rise to them are in action.

The exactly opposite explanation has been put forward by van der Hoeve. He believes that the insertion of an abnormal vortex vein at the posterior pole is the cause of the yielding of the ocular tunics, which produces myopia, just as the region of the normal vortex veins sometimes yields in equatorial staphyloma. This is a highly improbable conjecture.

Of all bodily structures the vascular system is perhaps the most capable of modification under altered circumstances, and this opens up the possibility of their occurrence rarely as a pure congenital abnormality. This would account for the cases in which they are found in emmetropic or hypermetropic eyes, though even in these cases the possibility of an abnormally small development of the ordinary vortex veins, or of a decreasing hypermetropia producing the same effects as a progressive myopia is to be remembered. It will be recalled that the usual explanation of many of the congenital abnormalities of vessels elsewhere in the body is the occlusion or maldevelopment of the normal channel and the enlargement of its collaterals, an explanation which can often be shown to be probable from the anatomical course of the abnormal trunk.

It is interesting to observe also that enlargements of the other anastomoses about the nerve-head are certainly not always congenital. Thus van Geuns reports a case in which an optico-ciliary vein developed during the course of an optic neuritis and disappeared afterwards, and there are other cases in which they have occurred with neuritis. The probable association of this with vascular obstruction in the nerve need hardly be pointed out. Indeed, van Geuns divides optico-ciliary veins into congenital and acquired, and believes that in the former the blood flows from the choroidal veins to the central and in the latter in the opposite direction. The enlargement of the third form of anastomosis, the little nets on the disc margin, is probably always acquired.

It will be seen from the above description that the term " choroido-vaginal " (chorio-vaginal, Oeller) is the best for these veins, as it describes their anatomical course. The term " posterior vortex " veins should be given up, as it implies that they are abnormally placed vortex veins, a supposition which is untenable both on practical and theoretical grounds.

LIEBRECH.—Atlas, 2nd ed., Pl. III, fig. 1.   CZERMAK.—Wiener klin. Woch., 1888. SCHOUTE.—A. f. O., xlvi, 2, 1898; Z. f. A., iii, 1900; in Nagel's Jahresbericht, 1903. AXENFELD.—In Nagel's Jahresbericht, 1898.   AXENFELD AND YAMASHITA.—B. d. o. G., 1900.   HAAB.—Atlas d. Ophthalmoscopie, fig. 80, 1900.   OELLER.—Atlas seltener ophthalmoscopische Befunde, Th. E, Pl. I, 1900.   VAN DER HOEVE.—A. f. A., xlvi, 1903.   VAN GEUNS.—A. f. A., xlviii, 1903.   THOMSON AND BALLANTYNE.—T. O. S., xxiii, 1903.   *COATS.—Ophth. Rev., xxv, 1906.

MICROPHTHALMIA AND ANOPHTHALMIA

Microphthalmia is the term used to designate the condition of smallness of the eye, which may in rare cases be otherwise normal. (*nanophthalmia*, dwarf-eye) or more commonly associated with congenital anomalies. *Microphthalmos* and other such cognate terms etymologically designate the patient who suffers from the deformity (Tweedy), and should be used in this sense.

Anophthalmia is the term used to designate the apparent absence of the eye, as observed clinically. Total absence of the eye is very rare. Cases of so-called anophthalmia include rudimentary eyes which either possess both epiblastic and mesoblastic structures, or more rarely meso-

FIG. 614.—MICROPHTHALMIA.

Mayou, T. O. S., xxiv. Specimen 1. From above downwards: eyelids and conjunctival sac, undifferentiated recti muscles inserted into rudimentary sclera, optic nerve, and in front of this lens and rudimentary globe.

FIG. 615.—MICROPHTHALMIA.

From the same specimen. Vertical section through eye. To the eft, entrance of optic nerve; to the right, distended anterior end of primary vesicle. Above the sclera, with tendon of superior oblique, the choroid and retinal pigment epithelium. The much vacuolated lens is in the centre, with ciliary body and retina behind. There is no sclerotic below. A large ciliary nerve is seen running forwards.

blastic structures only. Since the eye as a visual organ is dependent upon the development of the epiblastic structures, *i. e.* the primary optic
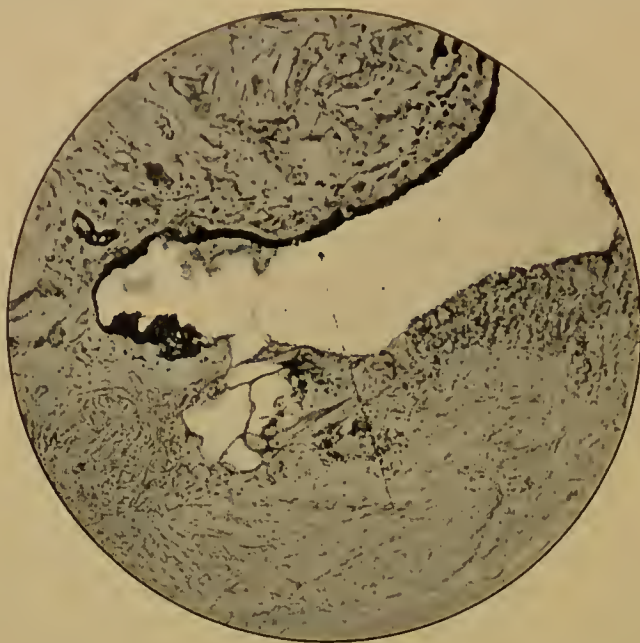
FIG. 616.—MICROPHTHALMIA.

From the same specimen. The entrance of the optic nerve. Above are the choroid and retinal pigment epithelium ; below, the nerve-fibres and commencement of the retina. Note the cleft between the two layers of the primary optic vesicle.
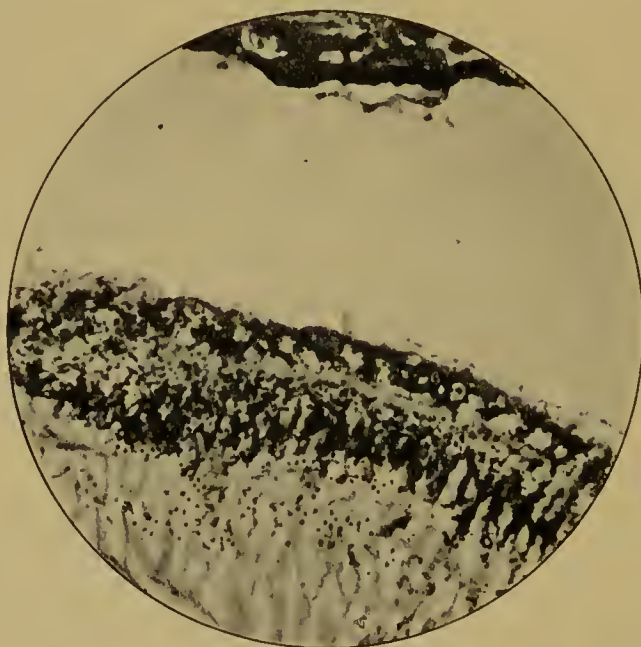
FIG. 617.—MICROPHTHALMIA.
From the same specimen. Above, the retinal pigment epithelium ; below, the retina.

vesicle, anophthalmia may be used in a more strictly scientific sense to denote the latter class (Treacher Collins and Parsons). Unfortunately,

it is impossible to apply this distinction clinically, since it depends upon accurate microscopical examination, and even then is often difficult. It
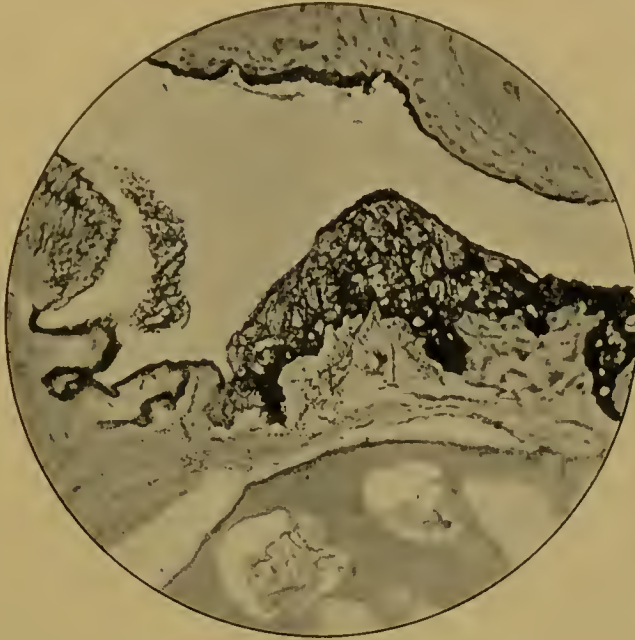
FIG. 618.—MICROPHTHALMIA.
From the same specimen. The ora serrata and ciliary body.
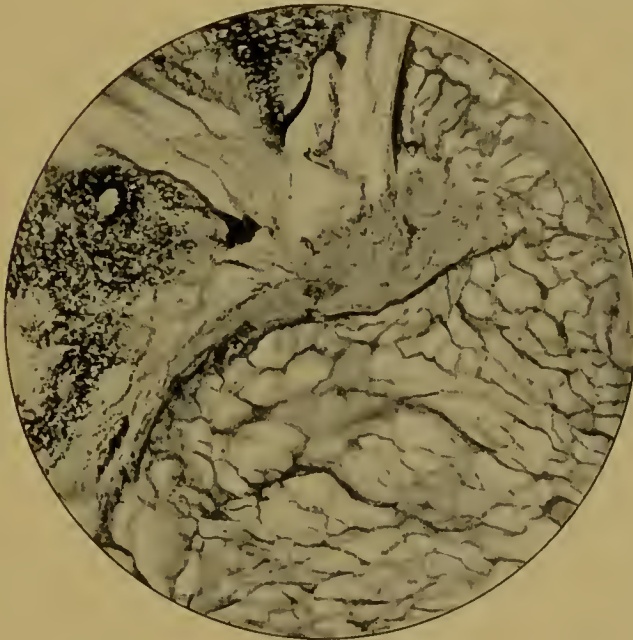
FIG. 619.—MICROPHTHALMIA.
From the same specimen. The lens, with capsule above, ending in coiled up mass.

will be seen that the first group is really only excessive microphthalmia, and indeed it is impossible and unnecessary to draw any very sharp line between the two conditions. For the sake of convenience of reference

to previously published cases, etc., it will be advisable to consider the conditions separately.
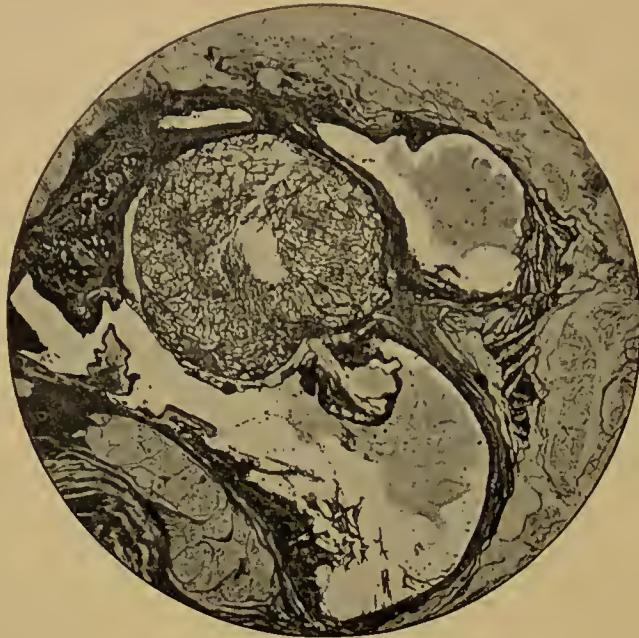
FIG. 620.—MICROPHTHALMIA.

From the same specimen. The distended anterior end of the primary optic vesicle, forming a cyst. The upper cyst is continuous with the lower around the inner side of the lens.
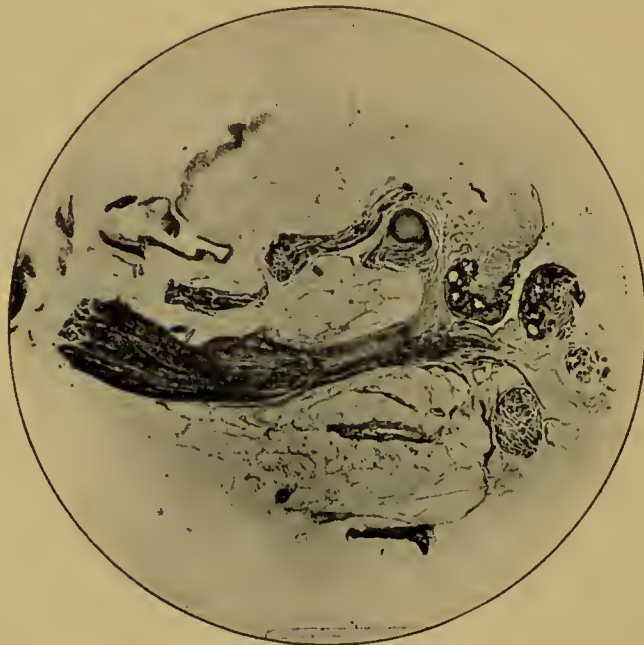
FIG. 621.—MICROPHTHALMIA.

From the same specimen, showing the arrangement of the muscles. Above, superior oblique, with tendon. In the middle, combined recti and levator palpebræ forming an aponeurosis around conjunctival sac. Below, transverse section of inferior oblique.

TREACHER COLLINS AND PARSONS.—T. O. S., xxiii, 1903. TWEEDY, T. O. S., xxiv, 1904.

Microphthalmia was early called attention to by Beer (1813), Pönitz (1822), Fischer (1827), Schön (1831), Himly (1843), Gescheidt,

FIG. 622.—MICROPHTHALMIA WITH CYST.
Mayou, T. O. S., xxiv. Specimen 2. Above, optic nerve; below, cystic coloboma, with folds of retina passing into it.

FIG. 623.—MICROPHTHALMIA WITH CYST.
From the same specimen. Showing arrangement of retina within cyst. The retinal pigment epithelium loses its pigment before entering the cyst, is then reduplicated on itself, and passes into more or less normal retina.

Cerutti, and others. Gescheidt observed cases with coloboma of the iris, arcus juvenilis, capsular cataract, etc. Himly early noted the very

common flattening of the cornea as well as atresia of the pupil (syni-
zesis), Cerutti concomitant defects in the brain—hemicephaly, and
Seiler hydrocephalus.

FIG. 624.—MICROPHTHALMIA WITH CYST.

From the same specimen.   Section through the disc, showing the lens distorted
and drawn out of place by atypically developed vitreous.
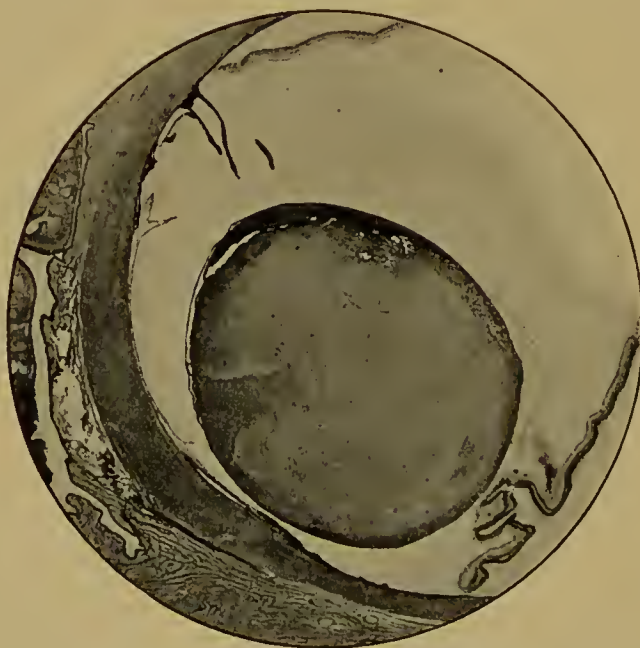
FIG. 625.—MICROPHTHALMIA WITH CYST.

From the same specimen.   Showing anterior part of globe, with ill-developed
iris and ciliary body, dislocation of lens, and folded retina.

Nanophthalmia, or smallness of the eye without other defect, has
been observed by Landesberg, Hess, Martin, van Duyse, and others;

FIG. 626.—MICROPHTHALMIA WITH CYST.

From the same specimen. Showing condition of ciliary body, iris, and lens below. Note the backward direction of the primary folds of the ciliary processes. The iris has not separated from the cornea, and the vascular sheath of the lens is still present.

FIG. 627.—MICROPHTHALMIA.

Mayou, T. O. S., xxiv. Specimen 3. Anterior part of globe, with mass of adipose tissue, partly surrounded by retina, which is detached and pushed inwards by very extensive cystic changes in the choroid.

the condition in any extreme degree is rare (Manz). It is met with in dwarfs as part of general microsomia.

FIG. 628.—MICROPHTHALMIA.

From the same specimen. Showing posterior part of globe, with same mass of adipose tissue.

FIG. 629.—MICROPHTHALMIA.

From the same specimen. Showing colloid degeneration of the choroid.

The commoner form of microphthalmia is associated with short and narrow palpebral aperture, short lids, and small orbit. The upper lid

can often be only partially raised (blepharoptosis congenita). It is
frequently unilateral. The same side of the face and even of the whole

FIG. 630.—MICROPHTHALMIA.
From the same specimen. The retina, hyaloid, and atypically developed
vitreous (adipose tissue).
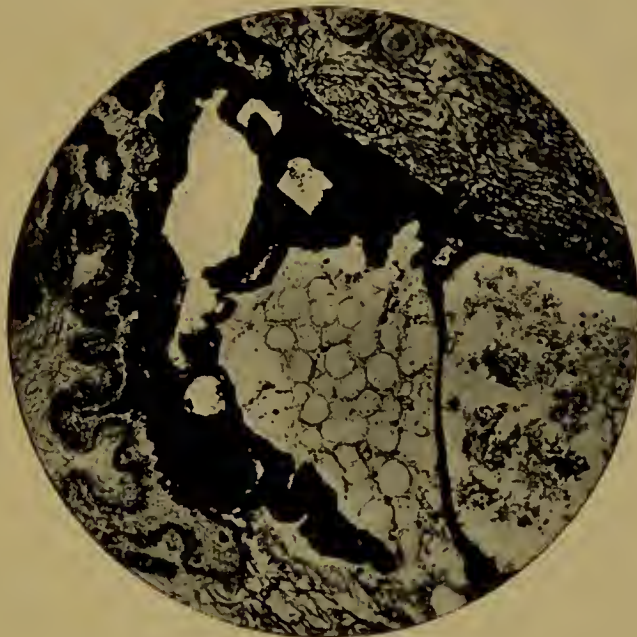
FIG. 631.—MICROPHTHALMIA.
From the same specimen. The ciliary body, showing the adipose tissue in the
situation of the suspensory ligament of the lens.

body may be diminished in size (*cf.* Rählmann). Microcephaly (Pflüger,
Hirschberg), occipital encephalocele (Schilling and Giulini), idiocy, and
other bodily deformities occur—*e. g.* polydactyly.

The globe nearly always moves well, showing that the musculature is fairly normal; nystagmus and strabismus are common.

The size of the globe shows every gradation to anophthalmia. The cornea is small (microcornea) and flat; it may be clear or show streaks or tongue-like patches of opacity, or be opaque and vascular; it may be absent, or replaced by a dermoid (Hanke). The anterior chamber is small, and the lens is often cataractous and may be shrunken and dislocated, or show colobomata. Seclusion and occlusion of the pupil occur, but the commonest anomaly of the iris is typical coloboma, in which case the cornea is oval with the long axis vertical. There may be persistent pupillary membrane (Bernheimer, Martin, Meyer, van Duyse), corectopia (Krückow), aniridia (Berthold, Page): even if the iris is fairly normal its mobility is usually greatly diminished. Coloboma of the choroid, often ectatic or forming large cysts (v. p. 887), and of the nerve, and persistent hyaloid artery are often found in cases examined anatomically. Light perception may be present, or amaurosis: vision is invariably reduced in all cases, except some of nanophthalmia.

There is no doubt that the eye may grow considerably in post-natal life (cf. Arlt); on the other hand, further diminution in size has been observed (Schaumberg).

The early authors regarded microphthalmia as a defect in development. Himly, v. Graefe, Hirschberg, Samelsohn, and others advanced the theory of intra-uterine inflammation; this was strongly supported by Deutschmann, whilst the developmental theory received warm support from Hess and Treacher Collins. Himly considered that heredity played an important part, and this is confirmed by the observations of Rava, Page (three generations with aniridia and microphthalmia), Mayerhausen (microphthalmia in two generations), Falchi, Martin, Reber (in three sisters), Samelsohn (transmission in the rabbit), and Deutschmann (transmission in the pig).

In favour of the inflammatory theory are the flatness of the cornea and shrunken appearance of the globe, marginal corneal opacities, regressive cataract (van Duyse), vascularisation of the cornea (v. p. 786), hyaline membranes in the angle of the anterior chamber and on the iris, anterior and posterior synechiæ, detached retina, colloid bodies, choroido-retinitis, bone-formation, retinitis pigmentosa (E. v. Hippel). Especially important is Krükow's case with congenital anterior staphyloma and absence of lens on one side and microphthalmia, congenital corneal opacity, and corectopia on the other, the brother having microphthalmia and congenital corneal opacities. Other similar cases have been recorded by v. Graefe, Manz, Himly, H. Müller, Höltzke, Tartuferi, Thalberg, etc.

On the other hand, the frequent presence of abnormalities in connection with the fœtal cleft, the absence of signs of past inflammation (lymphocytic infiltration, etc.) point strongly in the direction of arrested development with subsequent retrogressive metamorphoses. Even the presence of signs of inflammation must be interpreted with reserve, since they are often secondary and post-natal. Hess has brought forward the most important evidence of the developmental theory of

simple microphthalmia. In many of the cases the hyaloid artery, not infrequently displaced downwards, is surrounded by dense cellular connective tissue (Hess, Hänel, Bach, Thier, Dötsch, Ginsberg, Treacher Collins). The band starts from the disc or from the lower wall of the globe, and passes forwards to spread out on the back of the lens. It is vascular and composed of cells with long nuclei, mostly arranged parallel with the vessels and often extremely regular. Hyaline cartilage (de Vincentiis, Hess) and fat (Lange, Wiegels, Hanke, Mayou) have been seen in the tissue, and are probably due to atypical development of the connective tissue; the fat has been attributed to ingrowth of orbital fat (Leber), but the other explanation is more likely. Such dense fibrous tissue is not found normally in relationship with the hyaloid artery or lens sheath; according to Hess it is due to atypical development of the vitreous, and this in turn leads to defective expansion of the globe, whereby the lens is retained in an abnormally posterior position. E. v. Hippel, from his researches on the development of coloboma of the choroid in rabbits (v. p. 847), supports the view that defective secretion of fluid in the vitreous, an accompaniment of increased density of the tissue, is an indirect cause of deficient expansion of the globe. The retraction of the lens, which often lies far back near the lower wall of the eye, has been observed by v. Helmholtz, Arlt, Wallmann, Hess, Raehlmann, Treacher Collins, and others. Supporters of the inflammatory theory would naturally explain the position of the lens and density of the tissue to new formation of connective tissue with subsequent contraction, such as is so common in after life.

There is a definite group of cases in which there can be no reasonable doubt that the condition is one of congenital phthisis bulbi, e.g. the cases of H. Müller, A. v. Graefe, Schaumberg, Hirschberg, Mooren, Thalberg, Magnus, Rivaud-Landrau, Durlach, Samelsohn, Deutschmann, Brown-Séquard, E. v. Hippel. In one of Schaumberg's cases there was iridocyclitis with shrinking, and the eye continued to shrink after birth.

Reference has already been made to the condition of the lens in microphthalmia. Instead of being reduced in size, even to complete obliteration of all but the capsule (cf. Grolman, Vossius, Lange), it is occasionally disproportionately large (Bach). This may be well cited as an argument in favour of arrested development, since the lens is relatively enormous in the fœtal eye. Bach adduces it as the cause of the microphthalmia, the size of the lens preventing proper closure of the fœtal cleft; a comparison with normal conditions renders this theory highly problematical, and a comparison with the commoner conditions of the lens in microphthalmia makes it quite improbable.

It is stated that the lens may be absent altogether (Manz, H. Becker, Hanke): Manz attributes this to destruction after more or less normal development, H. Becker to absence of formation of the lens vesicle, and therefore of the anterior invagination of the primary optic vesicle, which is then only invaginated from below by the formation of the fœtal cleft. The former view is the more probable, though there are rare cases in which the lens is apparently situated below a non-invaginated primary optic vesicle. Mayou has described such a case

(Figs. 614–621); he attributes the condition to failure of the lens vesicle to hit off the primary outgrowth from the fore-brain.

I have recorded an extraordinary case of microphthalmia with

FIG. 632.—MICROPHTHALMIA WITH ORBITAL ENCEPHALOCELE.
Parsons and Coats, Brain, xxix.   Appearance of the patient at the age of seven months.
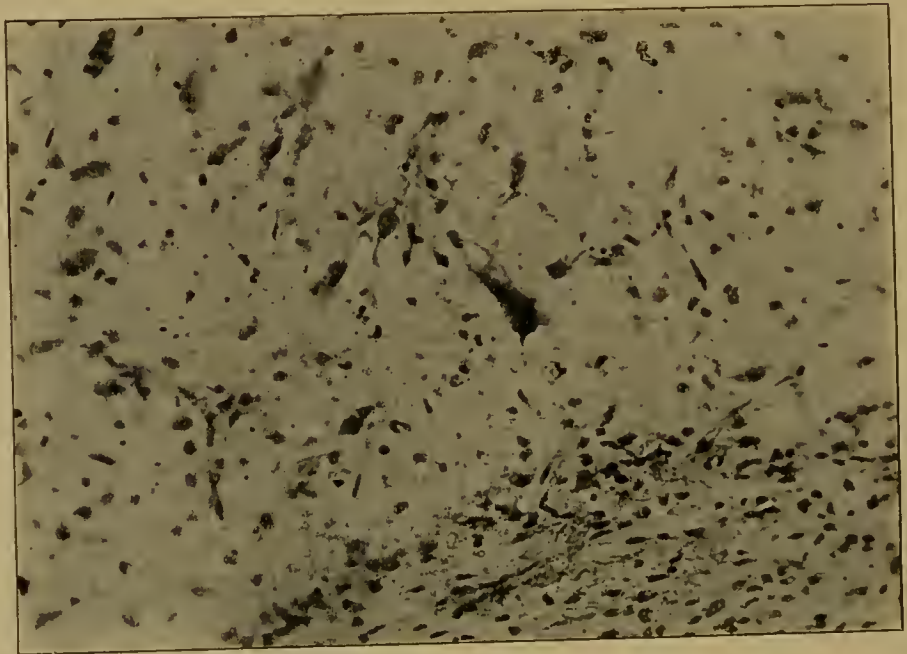

FIG. 633.—ORBITAL ENCEPHALOCELE.   × 230.
Parsons and Coats, Brain, xxix.   Section of the orbital encephalocele.

colobomata associated with an orbital meningo-encephalocele, the condition of the brain being unique (Parsons and Coats). A large mass of brain-substance, measuring 42 mm. by 25 mm. by 18 mm., was present in the orbit. The microphthalmic eye was displaced outwards, and the
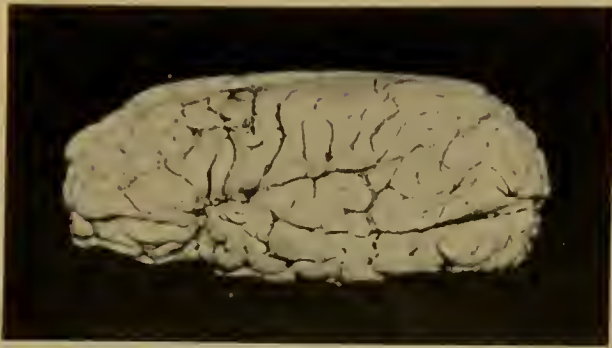
Fig. 634.—Brain from a Case of Microphthalmia, etc.
Parsons and Coats, Brain, xxix. Brain viewed from the left side—normal.
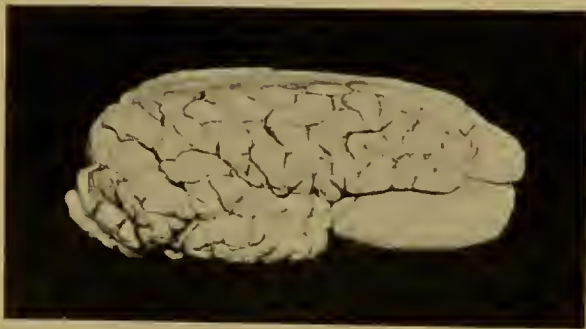
Fig. 635.—Brain from a Case of Microphthalmia, etc.
Parsons and Coats, Brain, xxix. Brain viewed from the right side, showing mass of brain-substance pressing frontal lobe upwards and temporo-sphenoidal lobe backwards.

Fig. 636.—Brain from a Case of Microphthalmia, etc.
Parsons and Coats, Brain, xxix. Brain viewed from below, with mass *in situ*.

dura mater covering the brain was intimately adherent to the flattened nasal surface of the eye. The encephalocele was connected by a pedicle which passed through the combined optic foramen and sphenoidal
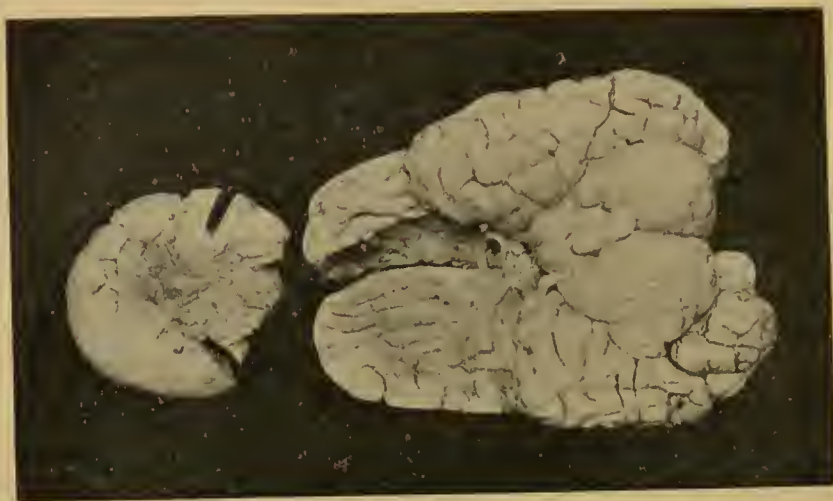
FIG. 637.—BRAIN FROM A CASE OF MICROPHTHALMIA, ETC.
Parsons and Coats, Brain, xxix. Brain viewed from below with mass displaced forwards, showing that the orbital convolutions are intact.
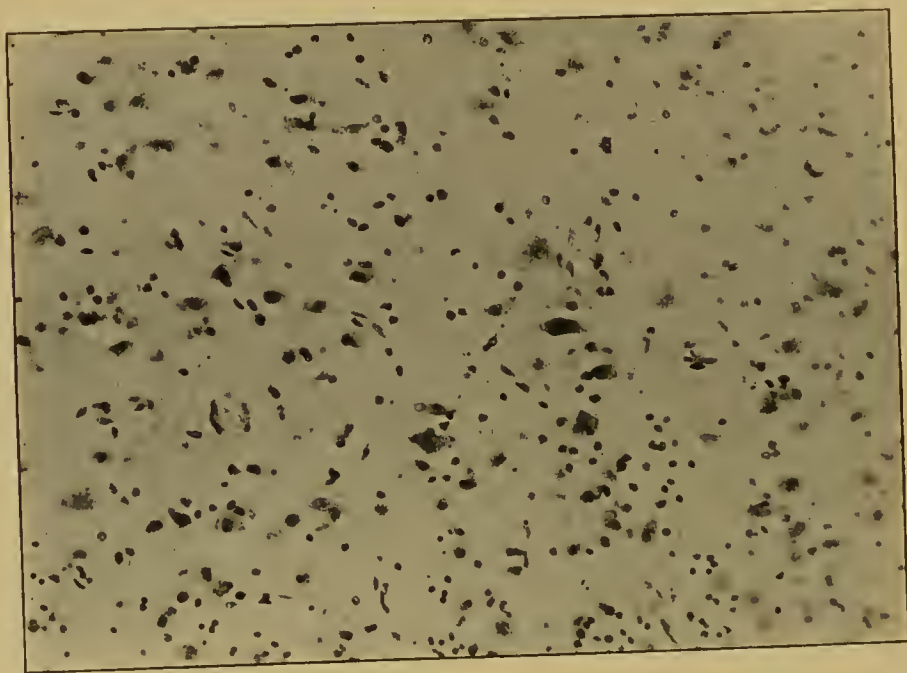
FIG. 638.—ISOLATED INTRA-CRANIAL MASS OF BRAIN-SUBSTANCE. × 230.
Parsons and Coats, Brain, xxix. Section of intra-cranial adventitious mass of brain-substance.

fissure with a large isolated mass of brain-substance, measuring 8·5 cm. by 8·4 cm. by 3·0 cm., lying under the right frontal lobe, which it pressed upwards, and in front of the temporo-sphenoidal lobe, which it pressed backwards (Figs. 635–638). The brain proper was quite intact.

having all the normal convolutions. It is probable that the isolated mass was due to independent development of an offshoot of the caudate region which became separated at an early stage of intra-uterine life.

In the eye, apart from the microphthalmia, there are three different congenital abnormalities. On the nasal side there is a large staphylomatous bulging; this is probably due to the pressure of the encephalocele, the bulging taking place at the interval between two convolutions upon its surface. There was a large coloboma of the optic nerve : the probable mode of development is indicated in the diagrams (Figs. 592, 594, 595, v. p. 834). Finally, there was a coloboma at the macula, represented only by absence of the pigment epithelium of the retina.

BEER.—Das Auge, Wien, 1813. Pönitz.—Dresdener Z. f. Natur- u. Heilkunde, ii, 1822. Schön.—v. Ammon's Zeitschrift, i, 1831. Fischer.—Hufeland's Jl., 1827. Himly. —Ophth. Beobachtungen ; Krankheiten u. Missbildungen d. menschl. Auges, i, 1843. Gescheidt.—v. Ammon's Z., i, 1831 ; ii, 1832. Cerutti.—v. Ammon's Z., ii, 1832. Landesberg.—K. M. f. A., xxiv, 1886. *Hess.—A. f. O., xxxiv, 3, 1888 ; xxxvi, 1, 1890 ; xxxviii, 3, 1892. Martin.—Dissertation, Erlangen, 1888. van Duyse.—Encyclopédie franç., ii, Paris, 1905. Manz.—A. f. O., xxvi, 1, 1880. Raehlmann.—Bibliotheca med., Stuttgart, 1897. Pflüger.—A. f. A., xiv, 1884. Hirschberg.—A. f. O., xxii, 3, 1876 ; C. f. A., v, 1881. Schilling and Giulini.—Münch. med. Woch., 1892. Bernheimer.— A. f. A., xxviii, 1894. Meyer.—C. f. A., xx, 1896. Krückow.—A. f. O., xxi, 2, 1875. Berthold.—Berliner klin. Woch., 1878. Page.—Lancet, 1874. Schaumberg.—Dissertation, Marburg, 1882. v. Graefe.—A. f. O., ii, 1855. Deutschmann.—K. M. f. A., xix, 1881. *Treacher Collins.—T. O. S., xiii, 1893. Ravá.—Ann. di Ott., ix, 1880. Mayer-hausen —C. f. A., vi, 1882. Falchi.—Ann. di Ott., xiii, 1884. Reber.—Ann. d'O., cxix, 1898. Samelsohn.—C. f. d. med. Wissenschaft, 1880. E. v. Hippel.—In G.-S., 1900 ; A. f. O., lv, 3, 1903. H. Müller (1859).—Gesammelte Schriften, Leipzig, 1872. Höltzke. —A. f. A., xii, 1883. Tartuferi.—In Nagel's Jahresbericht, 1884. Thalberg.—St. Petersb. med. Woch., 1883. Hänel.—Dissertation, München, 1885. Dötsch, Ginsberg. —A. f. O., xlviii, 1, 1899. de Vincentiis.—Ann. di Ott., xiv, 1885. Lange.—A. f. O., xliv, 1, 1897. Wiegels.—A. f. O., l, 2, 1900. Mayou.—T. O. S., xxiv, 1904. v. Helmholtz. —A. f. O., iii, 2, 1857. Arlt.—Lehrbuch, ii, 1854. Wallman.—Z. d. Ges. d. Wiener Aerzte, 1858. Mooren.—Fünf Lustren ophth. Wirksamkeit, 1882. Magnus.—A. f. A., xii, 1883. Rivaud-Landrau.—Ann. d'Oc., xxxvii, 1857. Durlach.—Dissertation, Bonn, 1882. Brown-Séquard.— Comptes rendus, xciv, 1882. Vossius.—B. d. o. G., 1896. Bach.—A. f. O., xlv, 1, 1898. H. Becker.—A. f. O., xxxiv, 3, 1888. Harman, Bronner. —T. O. S., xxii, 1902. Hanke.—A. f. O., lvii, 1, 1903. Parsons and Coats.—Brain, xxix, 1906.

Microphthalmia with orbital cyst.—When colobomata of the choroid are excessively ectatic definite cysts are formed, and there is then invariably more or less microphthalmia. The eye is often so small that anophthalmia is described.

The condition was first accurately discriminated by Arlt (1858), as the result of two anatomical examinations by Wallmann. de Wecker (1876) reported a case without giving an explanation, and another was recorded in the same year by Chlapkowski. Talko saw seven cases between 1877 and 1880, but thought that the cysts were not in direct communication with the eye : he considered that they were intra-uterine cysts which prevented the development of the globe. Gayet (1880) accepted the theory of his pupil Cusset that they were dermoid cysts developed in relation with the branchial cleft.

The condition is usually bilateral, and the globe can generally only be made out on careful examination or not at all clinically. The palpebral aperture is narrow, and the mobility of the lids is defective.

The lower lid is pushed forwards by a spherical tumour which gives well-marked fluctuation : the lid is stretched and bluish. It is possible to transilluminate the cyst. There is some ectropion of the lower lid,

FIG. 639.

FIG. 640.
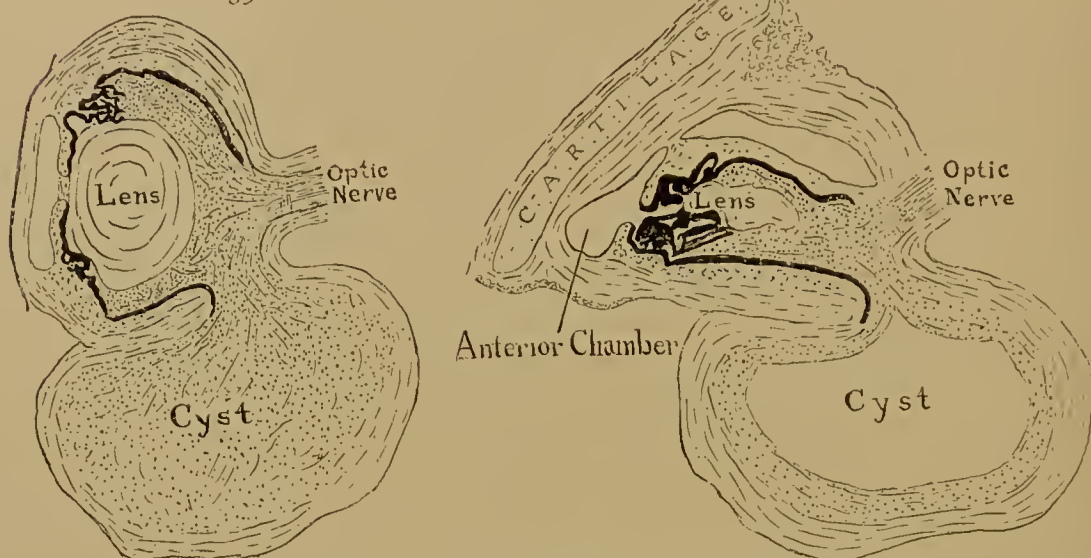
FIGS. 639 AND 640.—MICROPHTHALMIA WITH CYST.
Treacher Collins, T. O. S., xvii.

whilst the upper is usually turned in, so that the lashes irritate the conjunctiva. On separating the lids the conjunctiva bulges forward, no globe is seen as a rule, but palpation reveals a small hard nodule which undergoes spontaneous movements.
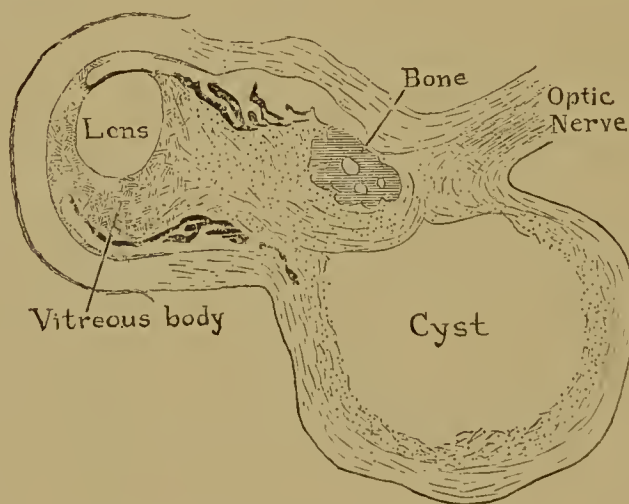
FIG. 641.—MICROPHTHALMIA WITH CYST.
Treacher Collins, T. O. S., xvii.

Rarely the eye is so large as to be quite recognisable (Hess. Ginsberg), and occasionally the cystic development involves the whole orbit without forming a specially definite protrusion of the lower lid.

Fluid may be drawn off from the cyst and is found to be clear, alkaline, and albuminous (van Duyse).

Anatomical examination has proved beyond dispute that the cyst is

Fig. 642.—Microphthalmia with Cyst.
Cruise, T. O. S., xxv.   Diagram of eye showing cystic coloboma, and fibrous band holding the lens back.

in definite communication with the eye (Ewetzky, Mayer, Tillaux. Lang, Rubinski, Czermak, Gallemaerts, Kundrat, Bernheimer, de Lapersonne, Fromaget, Mitvalsky, Becker, Hess, Treacher Collins,
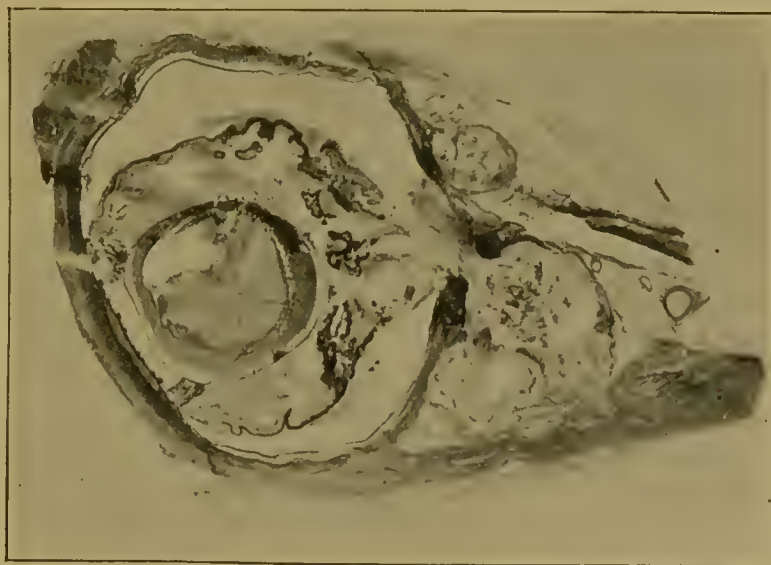
Fig. 643.—Microphthalmia with Cyst.
From a specimen by Fuchs.

Bach, Ginsberg, van Duyse).   Every gradation may be met with from the ectatic coloboma of the choroid, more especially those situated near the disc (Manz, Bock, Görlitz), and the fully developed cyst.

There are two chief theories as to the pathogenesis of these cysts, associated respectively with the names of Arlt and Kundrat. Arlt's is the generally accepted theory, viz. that the cyst is due to extreme development of ectasia in the neighbourhood of a defectively closed foetal cleft. Kundrat's theory, which has been adopted by Czermak and Mitvalsky, is that the cyst is formed from the non-invaginated primary optic vesicle. The case which Kundrat examined was one in which the interior of an extremely small eye was filled almost completely by the lens; there was no vitreous. A cleft below the disc led into multiple cystic spaces, which were lined with a glioma-like material, and were surrounded by embryonic tissue containing cartilage. Kundrat considered that this embryonic tissue was vitreous, that the

FIG. 644.—MICROPHTHALMIA WITH CYST.
Treacher Collins, T. O. S., xiii. *s*. Suspensory ligament of lens stretched and attached to elongated ciliary processes. *r*. Retina, much folded. *f*. Fibrous tissue in vitreous holding lens back. *p*. Point where choroid ends and retinal epithelium ceases to be pigmented.

primary optic vesicle extended forwards to the surface epiblast, so that invagination by the lens was possible, but that no invagination below occurred, the vesicle growing diffusely into the orbit and producing the cysts. This theory is held to explain the occasional inversion of the retina in the cysts (*v. infra*).

Microscopically the cysts have a fibrous tissue wall derived from the sclerotic, but this may be absent (de Lapersonne, E. v. Hippel). They communicate with the interior of the globe by an opening which is usually small but varies in size. They are lined by representatives of one or both layers of the secondary optic vesicle. The choroid is absent over the cyst wall, or extends only a short distance into it. The vitreous often passes through the orifice into the cyst.

The condition of the two layers of the retina in the cysts is important. The pigment epithelium is much altered, forming a somewhat laminated, unpigmented layer of cellular tissue. The retina proper is

FIG. 645.—MICROPHTHALMIA WITH CYST.

Treacher Collins, T. O. S., xiii. Posterior part of same eye. 1. Protrusion of retina through gap in sclerotic. 2. Point where the choroid ceases, and where retina and pigment epithelium are adherent. 3. Part where the pigment epithelium is apparently replaced by retinal tissue.
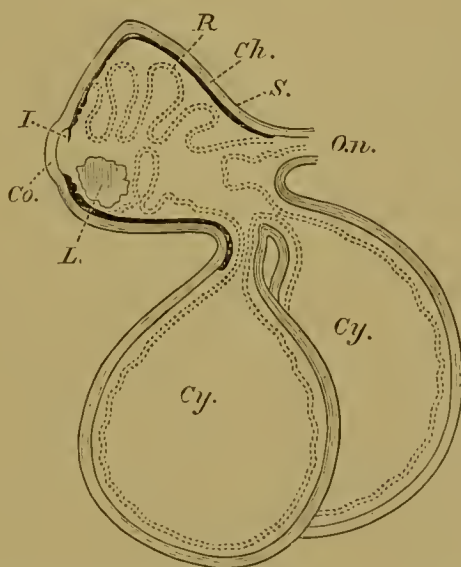

FIG. 646.—MICROPHTHALMIA WITH CYST.

Treacher Collins, T. O. S., xiii. Co. Cornea. I. Iris. L. Lens. R. Retina. Ch. Choroid. S. Sclerotic. O.n. Optic nerve. Cy. Cyst.

folded, especially near the orifice, but also lines the cyst. It may be well developed, so that the layers are quite distinguishable. It is found that in some cases the retina lies as in the eye (Hess, Rindfleisch, Treacher Collins), whilst in others it is inverted, showing so-called

"perverse" arrangement—*i. e.* the outer layers are directed towards the interior of the cyst (Rubinski, Mitvalsky, de Lapersonne, Czermak).

The eye shows all varieties from fairly good development to extreme minuteness. The retina may have escaped, as well as the vitreous, the fœtal cleft being widely open (*cf.* Mitvalsky). The conditions, indeed, are those found in microphthalmia and anophthalmia.

The "perverse" arrangement of the retina does not necessarily prove the origin of the cyst from the primary optic vesicle, as thought by Mitvalsky. Indeed, it becomes difficult then to explain the condition of the eye, so that Mitvalsky had recourse to partial invagination of the primary vesicle. Gallemaerts considered that the retina after the formation of the secondary optic vesicle became partially turned inside out, like the finger of a glove, the inverted portion being pressed out into the cyst through the soft tissue in the still open cleft. Pichler explains the perverse arrangement by prolapse of the fold of retina at one of the lips of the cleft. This theory is supported by the more recent researches of E. v. Hippel on the genesis of choroidal colobomata. Purtscher and Snell have described congenital cysts of the upper lid, but as there was no microscopical examination it is doubtful if they were of the type under discussion. Pichler conjectures that such cysts, as well as congenital serous cysts of the iris, may be due to overgrowth and prolapse of the anterior lip of the secondary optic vesicle.

Ginsberg has advanced the hypothesis that the cysts are due to nipping off of a knuckle of the secondary optic vesicle by mesoblast, so that it becomes incarcerated, though still in connection with the eye; under the intra-ocular pressure it expands. This theory would explain cysts in any direction. Considering the number of cases of atypical colobomata, it is surprising that atypical colobomatous cysts are so rare.

Hydrocephalus is sometimes found in these cases (Virchow and Bernheimer, Rindfleisch, van Duyse). Rindfleisch explained the condition of the eye by pressure from the brain, but, as E. v. Hippel points out, the eye lies in front of the orbit until the third month and is well protected from pressure behind.

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Anophthalmia.—Anophthalmia is generally bilateral—64 cases to 23 (E. v. Hippel). In cases of monophthalmia the eye was normal 15 times, showed microphthalmia 4 times, coloboma of the iris and choroid once, hypermetropia and nystagmus once, and greyness of the optic nerve sheath once. In one case coloboma of the lid and a nævus of the conjunctiva were present on the anophthalmic side (v. Hasner).

The palpebral aperture may be absent, but is generally small, opening into a conical cavity lined with conjunctiva. At the apex of the sac there is usually a soft nodular mass, which is the rudimentary eye. The lids and orbits are seldom absent (Klinkosch, Rudolphi, Sprengel, Seiler), but almost always very small. There is often ankyloblepharon. The cilia are scanty, the puncta lacrymalia often closed. The lids are

FIG. 647.—ANOPHTHALMIA AND MICROPHTHALMIA.
Treacher Collins and Parsons, T. O. S., xxiii. From a chick, showing the microscopical appearances of a vertical section through the chick's head traversing both orbits, under a low power. A malformed microphthalmic eye is shown in the left orbit. Deep in the right orbit is a ring of hyaline cartilage with some irregularly pigmented tissue, like that of the choroid, in its interior.

generally turned inwards. There is frequently a note of purulent conjunctivitis at birth (Wicherkiewicz, Braun, Kroll, Hilbert, Durlach. E. v. Hippel). In the last case at the age of 7 weeks a pure culture of non-virulent pneumococci was obtained from the conjunctival secretion.

Other concomitant anomalies are facial asymmetry (Landesberg), epicanthus (Lafosse), hare-lip (Huth), absence (Schenk, 1609) or malformation (Zimmermann) of the ear, malformations of the heart (Michel) and brain.

Anatomical examination has been carried out in the cases of Schmidt and Malacarne, Davy, Sissa, Bartscher, Röder, Gradenigo, Strawbridge, Zimmermann, and Spiller; microscopical in the cases of

v. Michel, Haab, Wedl and Bock, W. de Bary, Albrecht, van Duyse, Sgrosso, Bietti, Treacher Collins and Parsons, Hanke, Mayou.

The extrinsic muscles are usually present, though they may be badly differentiated from each other (*cf.* Mayou); this explains the spontaneous movements to which the nodule in the orbit is susceptible. The muscles are inserted either into the rudimentary eye or into the subconjunctival fibrous tissue. The lacrymal glands are almost invariably well developed. The nerves are nearly always seen in cases in which the muscles are present. Bartscher records absence of the oculomotor nerve and ciliary ganglion, Gradenigo of the latter and all the ciliary nerves. The optic foramen is narrowed or obliterated.
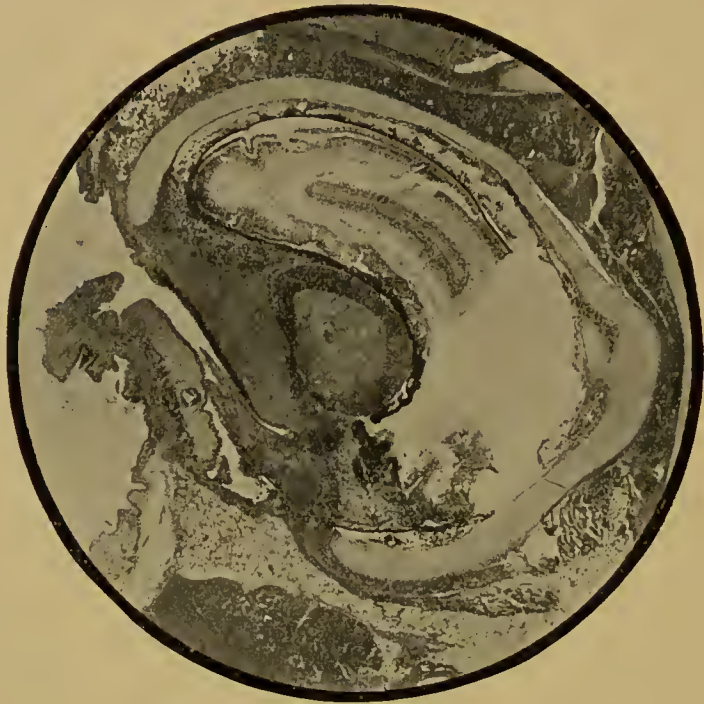
FIG. 648.—MICROPHTHALMIA.

From the same specimen, showing the left microphthalmic eye under a higher power. The adhesion of the lens to the posterior surface of the cornea is well depicted, also the extension of the upper part of the iris and ciliary body round the posterior surface of the lens, and the arrested development of the iris below.

There is nearly always aplasia of the optic nerves (*v.* p. 812); they may be represented by a fibrous cord. They may look fairly normal from the globe to near the optic foramen, dwindling then into a fine filament. In other cases the optic tracts, chiasma, and nerves are all absent or quite rudimentary, and the external geniculate body, optic thalamus, and corpora quadrigemina may be absent or ill-developed. Other, more extensive, malformations of the brain have also been reported.

There seems to be no case on record in which a microscopical examination of the orbital contents was made and where the mesoblastic structures of the eye were found to be entirely absent. There are several in which the rudimentary eye contained only mesoblastic

structures (Wedl and Bock, de Bary, Albrecht, v. Michel, Sgrosso, van Duyse, Bietti, Treacher Collins and Parsons, Hanke). The essential element of an eye is a nervous mechanism which serves to receive visual sensations for transmission to the brain : all the other tissues connected with and surrounding such a mechanism are merely subsidiary. Anophthalmia in the restricted sense may be reserved for those cases in which the epiblastic elements are absent and the eye is represented only by mesoblastic structures (Treacher Collins). Where both are present the condition is microphthalmia, no matter how small the eye may be.

As regards the pathogenesis of anophthalmia it must be due either to

FIG. 649.—ANOPHTHALMIA.
From the same specimen, showing the ring of hyaline cartilage from the right orbit more highly magnified, and the character of the tissue contained within it.

non-development of the eye or to destruction of the eye during intra-uterine life. In the rare cases in which no trace of an eye (*e. g.* Strösse, Hess, Fischl) or no trace of the epiblastic elements (*e. g.* Treacher Collins and Parsons) can be found on microscopical examination it is most probable that the primary optic vesicle has never budded out from the fore-brain. It is improbable, however, that this explanation applies to most of the cases, otherwise the orbit and eyelids would be absent more frequently (E. v. Hippel). v. Michel thought that the main cause of the condition was to be found in defective development of the brain : the occasional absence of the olfactory lobes (Davy, v. Michel) tends to support this view. On the other hand, the defects in the visual tracts may be secondary, or both may be due to a common cause.

Many of the cases, and all those with orbito-palpebral cysts, are merely extreme cases of microphthalmia (q. v.). Others show signs of inflammation, especially purulent discharge at birth (Wicherkiewicz, Braum, Kroll, Hilbert, Durlach, Haab, Hoppe, E. v. Hippel). It is not always certain that the infection is not intra- or post-partum (Hoppe), but it is extremely likely that some cases are due to intra-uterine inflammation, followed by shrinking of the globe.

It is possible that pressure of the amnion may be responsible for atrophy in some cases, and traumatism has been adduced in others (Hoederath).

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Cyclopia.—In cyclopia or synophthalmia an apparently single eye is found in the middle of the lower part of the forehead, rather above the normal position for the root of the nose. As the term "synophthalmia" indicates, the eye is really composed of the elements of the two eyes, variously developed and intimately fused. The condition is part of a widespread malformation, involving the brain, orbits, and face, and invariably leading to early death, usually immediately after birth, rarely from six weeks or eighteen months to ten years (Schön, Panum).

Cyclopia is not very uncommon, especially in pigs. The four lids bound a rhombic space, with rounded upper and lower angles : the pal- pebral aperture is usually, but not always, much wider than it is high, and some of the cornea is generally uncovered. The lids show normal structure, the caruncle is present, the lacrymal passages vary in different cases.

Above the eye there is usually a peculiar snout-like projection, which has often been mistaken for a misplaced penis : it has a knob at the end and is perforated by a blind canal. This proboscis is a rudimentary nose, and often contains rudiments of the nasal bones in the base ; it is due to the fronto-nasal processes being pushed forwards and upwards (Dareste). A small nasal aperture below the orbit has been described by Dursy, but this is the exception.

Other malformations, besides microcephaly, hemicephaly, and exencephaly, are astomia, malformation of the heart, and spina bifida.

Bock has classified the following degrees of the abnormality : (1) the eyes, each in its own orbit, are nearly approximated, the nasal aperture being single and very small ; (2) the eyes are so close together, each in its own orbit, that the nose is pushed upwards and assumes the form of a snout ; (3) there is one orbit containing two eyes and two optic nerves, the sclerotics being fused ; (4) the optic nerves are more closely approximated, the common scleral tissue is thinner, whilst the cornea, iris, lens, and vitreous are paired ; (5) the cornea is single, the iris, choroid, retina, and vitreous are paired, and the optic nerves are separated by a thin fibrous layer ; (6) cornea, sclera, choroid, retina, and optic nerve

FIG. 650.—CYCLOPIA.

Mayou, T. O. S., xxvi. Specimen 3. Cyclops with apparent anophthalmia (really an extreme degree of microphthalmia) with partial fusion. Two primary and secondary optic vesicles were present. There was a large mass of cartilage within the globe. (Inclusion from the fronto-nasal process, which is pushed forward to form the proboscis.) The proboscis contained cartilage and a cavity lined with ciliated epithelium, which communicated within the surface through the opening seen in the photograph. The posterior part of the fused cerebral hemisphere was converted into a large cyst (local hydrocephalus), probably due to distension in very early foetal life.

are single, two lenses are fused in the middle. E. v. Hippel adds (7) one eye, without any paired structure (Peunow, Bock, van Duyse) : an apparently single lens may be found microscopically to be due to fusion of two (Gabriélidès).

The size varies from abnormally large to apparent anophthalmia, but there is always a rudimentary eye found microscopically. The nearest approach to anophthalmia is seen in Nieden's case, but the development of lids, conjunctiva, and orbits point to destruction after greater or less embryonic deposition (E. v. Hippel).

The globes are always fused at the site of the fœtal clefts, and here coloboma of the retina, choroid, and optic nerve, often with typical colobomatous cysts below the nerve (van Duyse), are commonly seen. van Duyse describes typical coloboma of the iris and ciliary body, a fibrous mass below such as has been found in microphthalmia, and coloboma of the choroid associated with isolated coloboma of the macula.

The common orbit is formed of the fusion of the two orbits by disappearance of the ethmoid, with the exception of the lamina cribrosa, which, however, contains no perforations. The normal cribriform plate, with crista galli, is always absent. It is unnecessary here to enter into details as to the component bones of the orbit, which vary in their rela-
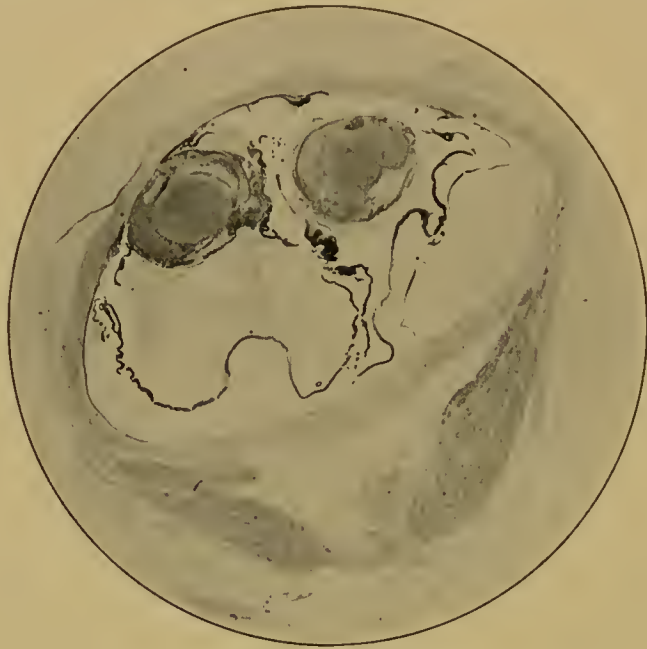
FIG. 651.—CYCLOPIA.

Mayou, T. O. S., xxvi. Specimen 2. A human cyclops showing two primary and secondary optic vesicles. The pigment cell layer of the retina is present except in the mesial line, where the retinæ come in contact; in this position the outer wall of the optic vesicle seems to have disappeared. Note the insertion of the muscles, situated far back.

tive arrangement in different cases. The extrinsic muscles are generally paired, but it may be impossible to isolate them completely.

The commonest abnormalities in the brain are absence of the olfactory lobes and chiasma, fusion of the two hemispheres, absence of the corpus callosum, corpus striatum, and trigonum. The optic thalami are almost always fused. There is very seldom a paired optic tract fusing into a single nerve. The optic nerve is often absent, in which case the ganglion-cells and nerve-fibres of the retina are undeveloped. Much more extensive changes in the brain may be present (cf. v. Monakow).

As regards the pathogenesis of cyclopia, Huschke (1832) held that the primary optic vesicles were unpaired when first developed from the

anterior cerebral vesicle; he considered that they failed to separate. More recent embryological research has disproved the fundamental data of his theory. Dursy and Ahlfeld attributed the condition to absence of the ethmoid, due to abnormal development of the median frontal process; such a cause would act too late in developmental life to account for the abnormality. Panum also considered that destruction of the intermediate parts or displacement as the result of defects in development in the neighbourhood would account for the condition.

Dareste frequently observed cyclopia during his teratological experiments. He discovered that at the time when the three primary cerebral vesicles are formed the anterior end of the central nervous system has a vertical cleft, which remains open until the optic vesicles are well
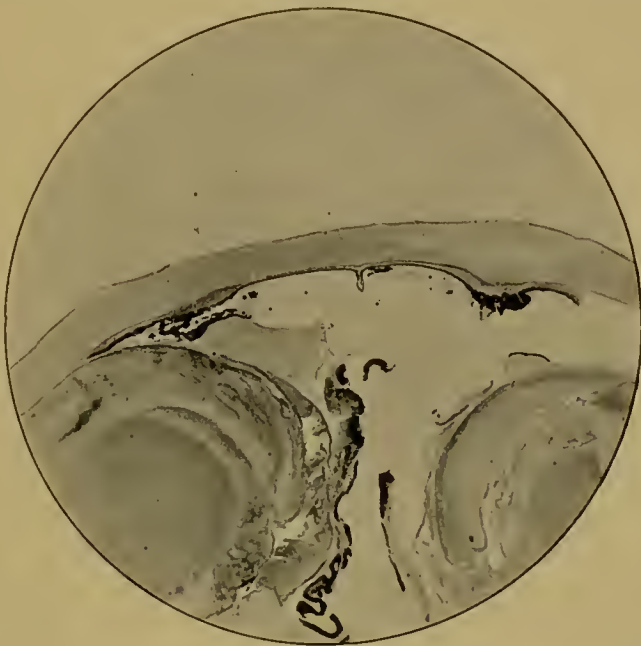
FIG. 652.—CYCLOPIA.

From the same specimen, showing the fused ciliary bodies in the mesial line. In the centre is a process to which the retina had been attached. Note the fœtal condition of the iris and the absence of the anterior chamber.

developed. He attributes cyclopia to too early closure of this cleft, brought about by pressure of the amnion, a cause which is also invoked by Taranetsky and van Duyse.

The fusion of paired organs or parts of organs has been observed in amphibian larvæ (*Rana esculenta, Bombinator igneus*) by Born. The earlier this occurs the more complete will be the fusion, so that all grades of cyclopia, including that reported by Gabriélidès, may be accounted for. Even complete mesial monophthalmia may be due to invagination by a single lens vesicle, and this is a more probable explanation than failure of one optic vesicle to develop, in which case it would not be mesial (E. v. Hippel). Early complete fusion of two lens vesicles within the eye would seem to be even more likely.

The occurrence of *diprosopia* is held by E. v. Hippel to support this theory. Between tetrophthalmic diprosopia (Marinotti and Sperino)

and triophthalmia there are various degrees of fusion of the heterologous halves of the face, so that all varieties of fusion of the two central eyes up to complete cyclopia are met with. Thus Macdonald found two corneæ and two irides in a single sclerotic in the median eye, and in Tschemolossof's case two median microphthalmic eyes were united by scleral fusion. Samelsohn described cases of diprosopia in the cat.

Mayou has recently described four cases of cyclopia, one in a dog and three in human fœtuses, one of the latter being a case of diprosopia. In the dog the lids formed an oval aperture, with a single caruncle below and a fold above this representing the plica semilunaris; no canaliculi could be found. The eye was large—7 mm. laterally, 3 mm. antero-posteriorly—and showed almost complete fusion. The
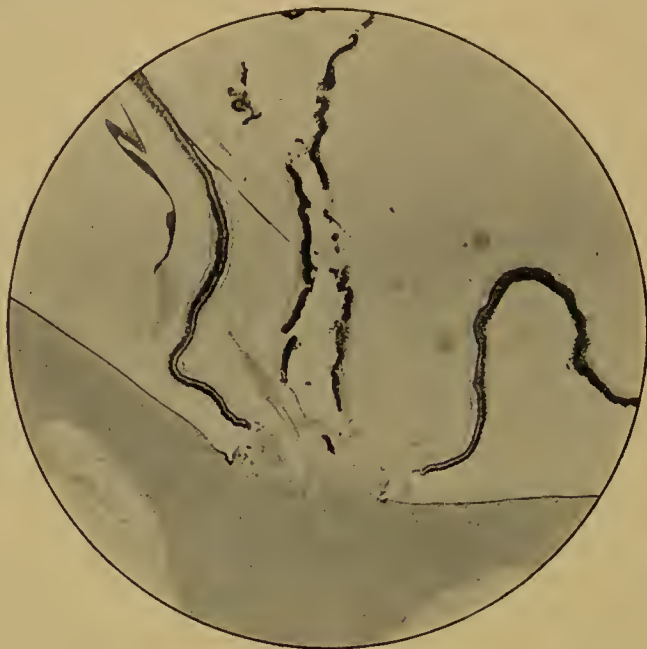
Fig. 653.—Cyclopia.
From the same specimen, showing the optic disc with two hyaloid arteries. The optic nerve was single.

cornea measured horizontally double its vertical diameter. The iris was applied to the cornea in its whole extent. The lens was single, large, normally situated, longer horizontally than vertically; the capsule was normal and the vascular sheath was present. The retina, ciliary body, and choroid were single. The optic nerves were fused as far back as the base of the brain, where they divided into two, one passing to the left, the other to the right hemisphere. Transverse section showed no differentiation into two nerves. The olfactory nerves were double, passing into the proboscis by a single aperture.

One human specimen showed complete absence of a proboscis. There were four puncta, two on each side in the lower lid; none in the upper lid. There was a single central caruncle below. The eye, measuring 2 cm. laterally and 1 cm. antero-posteriorly, was made up of two optic vesicles. The cornea, apparently single, was seen on section to be made up of two corneæ lying side by side. There were two

irides closely applied to the back of the cornea and to the side of the lens. Two sets of ciliary processes united in the mesial plane into a pigmented process to which the retina had evidently been attached. The ora serrata was in the fœtal condition. Two well-developed retinæ came in contact mesially, but the pigment epithelium was absent here. The disc was single, but there were two hyaloid arteries. The optic nerves were fused, and showed no differentiation microscopically. Two ophthalmic arteries passed through the single foramen at each side of the nerve, and the central retinal vessels were placed laterally to the nerve before entering it. There were no optic tracts and the olfactory nerves were absent.

Another specimen showed apparent anophthalmia; on dissection

FIG. 654.—DIPROSOPIA.

Mayou, T. O. S., xxvi. Specimen 4. A twin cyclops with fused heads. There was an exactly similar face on the other side. Although the eye was derived half from each fœtus, it was almost perfectly formed except for a coloboma of the nerve-sheath, there being only one primary and secondary optic vesicle. The canaliculi, which were present only in the lower lids, were fused into a single blind canal at their inner end.

fused microphthalmic globes were found, measuring 1·1 cm. laterally and 0·9 cm. antero-posteriorly. They lay side by side behind a single cornea. The sclerotics were differentiated except over a small area where the globes came in contact. In front a process of mesoblast passed backwards from the cornea. Attached by a pedicle of fibrous tissue to the fused corneæ was a mass of cartilage which bulged into the interior of one of the globes; it was doubtless part of a fronto-nasal process. The lenses were extremely small, surrounded by thick fibro-vascular capsules. No anterior chamber, iris, or ciliary processes could be made out. Two optic discs, separated by a process of mesoblast, gave rise to two hyaloid arteries. There was a single undifferentiated optic nerve, but no optic tracts. There was a single small olfactory

nerve. The occipital and temporo-sphenoidal regions of the brain were occupied by a large cyst.

The case of diprosopia was a double fœtus of nine months. The faces were united, with a mouth and one eye on each side—Janus-like—each with a proboscis above the eye. A single neck passed into two complete fœtuses below. Here each single eye represents the fusion of one eye of each fœtus. There were no puncta in the upper lids, but a single one in each lower lid leading to a canaliculus which ran downwards and inwards to unite with its fellow in the middle line, forming a single canal which ended blindly. One eye was examined and showed almost complete fusion into a fairly normal eye. It measured 1·5 cm. laterally and 1·4 cm. antero-posteriorly. The corneal diameter was 0·9 cm. horizontally and vertically. The iris was short, but separated from the cornea. The single lens showed some traces of a vascular capsule. The retina and choroid were single. A single disc showed a coloboma extending into the sheath. There was a single optic nerve, but no tracts. There was a single olfactory nerve to each face. The frontal lobes were fused. There were two cerebella, medullæ, and spinal cords.

SCHÖN.—Handbuch der path. Anat., 1828. PANUM.—Virchow's Archiv, lxxii, 1878. BOCK.—K. M. f. A., xxvii, 1889. PEUNOW.—In Nagel's Jahresbericht, 1889. GABRIÉLIDÈS.—A. d'O., xvi, 1896. NIEDEN.—A. f. A., xxii, 1890. v. MONAKOW.—Naturf. Vers. Frankfurt, ii, 2, 1896. HUSCHKE.—Müller's Arch. f. Anat. u. Phys., 1832. DURSY.—Zur Entwicklungsgeschichte des Kopfes, Tübingen, 1869. AHLFELD.—Die Missbildungen des Menschen, Leipzig, 1880. DARESTE.—Recherches sur la production artificielle des monstruosités, 1877; Ann. d'Oc., cvi, 1891. TARANETSKY.—A. f. A., xii, 1883. BORN.—Arch. f. Entwicklungsmechanik, iii, 1897. HESS.—A. f. O., xxxviii, 3, 1892. MARINOTTI AND SPERINO.—Internat. Monatsschrift f. Anat. u. Phys., v, 1888. MACDONALD.—Edin. Med. Jl., 1875. TSCHEMOLOSSOF.—Prager med. Woch., 1899. SAMELSOHN.—Berliner klin. Woch., 1881. VASSAUX AND VALUDI.—A. d'O., viii, 1888. *E. v. HIPPEL.—In G.-S., 1900. *VAN DUYSE.—A. d'O., xviii, 1898; Encyclopédie franç., ii, Paris, 1905. *MAYOU.—T. O. S., xxvi, 1906.

ANOMALIES OF PIGMENTATION

Albinism.—Albinism in the eye is part of a general defect in pigmentation in the whole body. It is more common in dark races than in light. Wafer is said to have observed the first albinoes in Panama at the end of the eighteenth century, and Blumenbach (1786) in Switzerland, attributing the red colour of the iris to its true cause.

Geoffroy St. Hilaire's classification into complete, incomplete, and partial albinism may be conveniently applied to the eye: incomplete albinism denotes generalised diminution of pigment without total absence, whilst partial albinism denotes complete or incomplete absence of pigment in parts of the eye, the remainder being normal.

In complete albinos the hair and eyelashes are devoid of pigment, and are usually fine and downy. There is marked photophobia, expressed by the lowered head and screwed-up eyes. On opening the eyes the conjunctiva is seen to be hyperæmic and the iris is red, the radial striations being much in evidence. There is nystagmus, and often strabismus. The pupil is small, enlarging little on shading, but showing great activity. Ophthalmoscopically the choroidal vessels are seen beneath the retinal, and there is no pigment between them: the

disc is only recognisable by the confluence of the retinal vessels (Mayerhausen).

Vision is subnormal, but the field of vision and colour sense may be normal. There is generally myopia, with or without astigmatism, or sometimes hypermetropia. The myopia may be due to increased curvature of the cornea (*e. g.* radius = 6·5 mm., Mayerhausen), but this is by no means constant (Manz).

Anatomical investigation has shown that the idea that the retinal epithelium is absent (Buzzi) is unfounded. In albino rabbits the epithelium contains no pigment, but in the human eyes examined there is always some pigment here, but it is entirely absent from the stroma.

Meckel and Mansfeld attribute albinism to arrest of development of pigment, Blumenbach and Siebold to psychical impressions during labour. Aubé pointed out consanguinity in the parents, but this is only occasional. Heredity plays a much more prominent part (*cf.* Mayerhausen).

As regards pathogenesis the time of development of the pigment in the eye is a matter of prime importance. Scherl has shown that pigment-formation occurs immediately after the development of the vascular system, and in direct relationship with it—*i. e.* at the end of the fourth week (v. Kölliker). In mammals, with an intra-ocular blood-supply, deposit of pigment first occurs on the inner face of the retinal epithelium, whilst in birds, with only an extra-ocular supply, it occurs on the outer side. The pigment is at first in solution, and later becomes solid; at an early period it contains iron (hæmosiderin, Neumann). The pigmentation of the choroid, on the other hand, occurs only shortly before birth (seventh month, Treacher Collins, Rieke) and is minimal at birth. It is not surprising therefore that cases of partial albinism may show improvement and increased pigmentation during the first few years (Seligsohn).

L. Müller has described a form of partial albinism as *vitiligo* of the iris. Here numerous small, rounded, or elongated white spots are dotted over the iris, and correspond with excavations in the stroma. The spots are found to be free from pigment on microscopical examination.

ARCOLEO.—Virchow's Jahresbericht, 1871. WAFER.—In Mansfeld, Ueber das Wesen der Leucopathie, Braunschweig, 1882. BLUMENBACH.—De oculis lucæthiopum et iridis motu, Göttingen, 1786; Handbuch d. vergleich. Anat., 1824. MAYERHAUSEN.—K. M. f. A., xx, 1882. MANZ.—In G.-S., ii, 1876. BUZZI.—In Seiler, Beobachtungen ursprüngl. Bildungsfehler, etc., Dresden, 1833. MECKEL.—Arch. f. Anat., u. Phys., 1826. SCHERL.—A. f. O., xxxix, 3, 1893. RIEKE.—A. f. O., xxxvii, 1, 1891. SELIGSOHN.—Art. Albinismus, Eulenberg's Real-Encyclopädie, i, 1880. L. MÜLLER.—B. z. A., vii, 1892.

Heterochromia is the condition in which the two irides are different in colour, or the iris of one eye has half or a sector of different colour from the remainder; the latter condition may be seen rarely in both eyes (bilateral heterochromia, dicorus). The sector is usually grey or blue, the remainder brown.

Blue eyes show normal pigmentation of the retinal epithelium, the stroma being deficient in pigment: hence the colour depends chiefly upon the pigmentation of the stroma, and especially of the anterior

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surface (Merkel), as well as upon the structure and density (Broca). Sym has pointed out that one parent is often fair, with blue eyes, the other dark.

Hutchinson has pointed out that heterochromia is associated with defects of structure as revealed by operation, and Malgat and Bistis showed that such eyes were especially subject to cataract. It is probable that these cases are not true congenital heterochromia, but that the alteration in colour of the iris is due to iridocyclitis, which leads to the development of complicated cataract (*v. infra*).

HUTCHINSON.—R. L. O. H. Rep., vi, 1, 1867; 4, 1869. MALGAT.— Rec. d'O., 1895. BISTIS.—C. f. A., xxii, 1898. SYM.—Ophth. Rev., viii, 1889. WEILL.—Z. f. A., xi, 1904. *FUCHS.—Z. f. A., xv, 1906.

Melanosis oculi.—Pigmentation of the conjunctiva (Vol. I, p. 110), cornea (Vol I, p. 249), sclerotic (Vol. I, p. 267), and iris (Vol. I, p. 331) have already been referred to incidentally.

Pigmentation of the *conjunctiva* in dark races has been investigated by v. Kölliker, Pergens, Steiner, Herbert, and others. Congenital pigmentation has been described by Liaras, Leber, Westhoff, and others, but it is not always certain that the condition was truly congenital.

Congenital deposits of pigment in the deeper layers of the *cornea* have been described by Krukenberg, Stock, and Thomson and Ballantyne; they are probably due to intra-uterine inflammation, with transference of uveal pigment to the cornea.

Patches of pigment in the *sclerotic* are common in lower animals. They have been described in man by v. Ammon, Liebreich, Hirschberg, Clavelier, Harman, and others. Slight pigmentation around the anterior perforating ciliary vessels is not very uncommon.

Congenital pigmentation of the *retina* has often been observed ophthalmoscopically (Jaeger, Stephenson, Batten and Holmes Spicer, Work Dodd, Juler, James, Roll).

I have had the opportunity of examining one such case microscopically, the pigment spots consisted of aggregations of very densely pigmented retinal epithelial cells.

Pigmentation of the *optic disc* was figured in Liebreich's atlas (1870). The disc is usually greyish-black. The condition was observed in two albinotic eyes by v. Forster. The disc may be surrounded by a wide ring of dense black pigment (Hilbert); this is probably due to heaping up of the retinal pigment epithelium at the edge of the disc, and is only an exaggeration of a condition frequently observed. There is often radial striation, as in Pick's case; here the disc had a black centre with a grey ring, outside which were masses of medullated nerve-fibres. This case disproves v. Forster's theory that the greyness is due to non-myelination. There are pigmented cells normally in the lamina cribrosa, commencing before the seventh week (Pick). This requires confirmation. Thomson and Ballantyne have described a pigmented coloboma of the disc.

v. KÖLLIKER.— Münch. med. Woch., 1883. PERGENS. — Ann. d'Oc., cxx, 1898. STEINER.—C. f. A., xxii, 1898. HERBERT.—Internat. Congress, Lucerne, 1904. LIARAS.— Rev. gén. d'O., 1898. LEBER.—B. d. o. G., 1898. WESTHOFF.—C. f. A., xxii, 1898. KRUKENBERG.—K. M. f. A., xxxii, 1899. STOCK.—K. M. f. A., xxxiv, 1901. THOMSON AND

BALLANTYNE.—T. O. S., xxiii, 1903. v. AMMON.—In G.-S., iv, 1876. LIEBREICH.—In G.-S., ii, 1876. HIRSCHBERG.—A. f. O., xxix, 1, 1883. CLAVELIER.—Rec. d'O., 1895. HARMAN.—T. O. S., xxv, 1905. STEPHENSON.—T. O. S., xi, 1891. BATTEN AND HOLMES SPICER.—T. O. S., xiv, 1894. WORK DODD.—T. O. S., xv, 1895. JULER.—T. O. S., xvi, 1896; xxii, 1902. JAMES.—T. O. S., xxi, 1901. ROLL.—T. O. S., xxii, 1902. PARSONS.— Internat. Congress, Lucerne, 1904. v. FORSTER.—K. M. f. A., xix, 1881. HIRSCHBERG.— C. f. A., vi, 1881. HILBERT.—K. M. f. A., xx, 1882. SCHLEICH.—K. M. f. A., xxiii, 1885. PICK.—A. f. A., xli, 1900 (Bibliography).

THE LACRYMAL APPARATUS.

Atresia of the puncta lacrymalia.—Zehender twice observed atresia of one or more puncta; another case is reported by Lafite-Dupont. The blockage is caused by an epithelial membrane; the canaliculi are patent. Cases of inflammatory or traumatic atresia are liable to be mistaken for the congenital condition, which is not very conclusively demonstrated.

ZEHENDER.—K. M. f. A., xxi, 1883. LAFITE-DUPONT.—Soc. d'Anat. et de Phys. de Bordeaux, 1895.

Absence of the puncta lacrymalia.—This has been observed twice in the lower puncta (Magnus) and once in all four puncta. In the former case the patient was 22 years old, in the latter 6. It is, therefore, doubtful if the condition is congenital. The canaliculi were said to be absent in each case, but this is insufficiently substantiated. Failure of the puncta to develop would be due to non-canalisation of the epithelial cord from which the canaliculi are formed. Sometimes a groove is formed along the course of the canaliculi instead of a tube.

MAGNUS.—K. M. f. A., xiii, 1875; C. f. A., iv, 1880. EMMERT.—A. f. A., v, 1875. MACNAUGHTON JONES, DOYNE.—T. O. S., xvii, 1897. JAMES.—T. O. S., xxii, 1902.

Supernumerary puncta and canaliculi.—This abnormality is not excessively rare, and usually affects the lower lid. The two puncta generally open into a common canaliculus, but sometimes there is a separate one opening independently into the lacrymal sac. The occurrence of traumatic fistulæ must be borne in mind in settling the diagnosis.

BEHR, MACKENZIE, v. GRAEFE.—In Mackenzie, Diseases of the Eye, 1856. FOLZ, ZEHENDER, STEFFAN, RAAB.—In Raab, K. M. f. A., xiii, 1875. BOCHDALEK.—Prager Vierteljahrsschrift, 1866. WEBER.—A. f. O., vii, 1860.

Absence of the lacrymal bone has been described by Barfurth and Zabel.

BARFURTH.—Sitzungsbericht d. naturf. Gesellschaft zu Rostock, 1899. ZABEL.—Dissertation, Rostock, 1900.

Absence of the lacrymal gland has been described as the rule in anophthalmia, but this is not the case. It was absent in a case of cryptophthalmia examined by van Duyse. Absence of lacrymation is no proof of absence of the gland.

VAN DUYSE.—Encyclopédie franç., ii, Paris, 1905.

Absence of the lacrymal sac and nasal duct.—Agenesis of the lacrymal sac alone has been reported by Beyer, absence of the nasal

duct by Carron du Villards, Otto, Travers, and others. Selenkoff and Landow describe two remarkable cases in which the lacrymal passages were absent, together with one side of the nose, which was replaced by a snout-like protuberance. Landow attributes the condition to amniotic pressure. Kraske and van Duyse and Rutten describe cases in which a canal led from the lacrymal sac into a hare-lip; the condition is associated with an unclosed facial cleft, with coloboma of the lid.

Beyer, Carron du Villards, Otto, Travers.—In Manz, G.-S., ii, 1876. Selenkoff.—Virchow's Archiv, 1884. Landow.—Deutsche Z. f. Chir., xxx, 1890. Kraske.—Arch. f. klin. Chir., xx, 1876. van Duyse and Rutten.—A. d'O., xvii, 1897. Vossius.—B. z. A., ii, 1891.

Fistulæ.—Fistulæ of the lacrymal sac have been repeatedly recorded. They may be unilateral (Schreiber) or bilateral and symmetrical (Wood, Hardesty). They have been attributed to arrest of development, and

Fig. 655.—Minimal Fissura Facialis.
Harman, T. O. S., xxiii.

minimal failure of the fissura facialis to close (Harman). This may be true of some cases, but they are probably more often of inflammatory origin. There is usually blennorrhœa of the sac. Adler attributes the fistula to arrested development and the blennorrhœa to fœtal inflammation, an unnecessary complication.

Mackenzie and Steinheim have described true lacrymal fistulæ involving the gland and opening on to the upper lid.

Scarpa.—Traité, iv. Agnew.—T. Am. O. S., 1874. Adler.—Bericht der k. k. Krankenhaus zu Wieden, 1878. Hardesty.—Med. and Surg. Reporter, xxxviii, 1878. Schreiber.—Jahresbericht d. Augenheilanstalt in Magdeburg, 1885. Hartridge.—T. O. S., xii, 1892. Wood.—A. of O., xxii, 1892. Mackenzie.—Diseases of the Eye, 1830. Steinheim.—K. M. f. A., xiii, 1875. Sperling.—Dissertation, Königsberg, 1899. Merlin.—Wiener. med. Woch., 1901. Grimsdale.—T. O. S., xxi, 1901. Lundsgaard.—In Nagel's Jahresbericht, 1902. Harman.—T. O. S., xxiii, 1903. Dalén.—Widmark's Mittheilungen, v, 1904. de Ridder.—Ophth. Klinik, 1905. Elschnig.—K. M. f. A., xliv, 1906.

Congenital dacryocystitis.—Blennorrhœa of the lacrymal sac at or very soon after birth is common, and is frequently mistaken for an

ordinary conjunctivitis. Pressure on the sac usually causes copious regurgitation of muco-pus. Congenital dacryocystitis may occur in several members of the same family (Trousseau, van Duyse), and lacrymal affections in parents and children are not uncommon (Nieden).

The condition is often, probably generally, due to want of complete canalisation of the nasal duct. This was observed anatomically in fœtuses and new-born children by Bochdalek, Vlacovitch, Ewetzky, and others, and has been demonstrated in a case of congenital dacryocystitis by Cirincione. The blockage is due to a mass of epithelial cells or a membrane (Peters) at the lower end of the duct. This accounts for the ease of cure in some cases by carefully passing a probe once.

TROUSSEAU.—Soc. franç. d'O., 1891. VAN DUYSE.—Soc. de Méd. de Gand, 1892; Encyclopédie franç. ii, Paris, 1905. NIEDEN.—C. f. A., viii, 1883. BOCHDALEK.—Prager Vierteljahrsschrift, 1866. VLACOVITCH.—In Nagel's Jahresbericht, 1871. EWETZKY.—A. f. A., viii, 1879; A. f. O., xxxiv, 1, 1888. CIRINCIONE.—Lavori della Clin. oc. di Napoli, iv, 1895. PETERS.—K. M. f. A., xxix, 1891.

CHAPTER XV

MYOPIA

Myopia is that dioptric condition of the eye in which, with the accommodation at rest, incident parallel rays come to a focus anterior to the light-sensitive layer of the retina. The first satisfactory definitions were stated by Kepler (1611) and Boerhave (1708).

Myopia may be due, theoretically, to any of the following conditions:

A. Abnormal length of the eye—*axial myopia*.
B. Abnormal curvature of the refracting surfaces—*curvature myopia*:
   (a) Too strong curvature of the cornea.
   (b) Too strong curvature of one or both surfaces of the lens.
C. Abnormal refractive index of the media—*index myopia*:
   (a) Too high index of the cornea or aqueous.
   (b) Too high total index of the lens, due to—
      (a) Too high index of the nucleus.
      (β) Too low index of the cortex.
      (γ) Both these causes.
   (c) Too low index of the vitreous.
D. Abnormal position of the lens—*i. e.* displacement forwards.
E. A combination of the above abnormalities.

Axial myopia is by far the commonest condition. Plempius (1632) first examined the myopic eye anatomically, and attributed the condition to lengthening of the part between the lens and the retina. Boerhave (1708) attributed it to the same cause, as well as to greater convexity of the cornea. Morgagni (1761) gave anatomical demonstration of the great length of the myopic eye. Guérin (1769) described an ectatic condition which foreshadows the staphyloma posticum of later authors. Richter (1790) again attributed myopia to axial lengthening; Scarpa (1807) and Ritterich (1842) drew attention to the shape of myopic eyes, but apparently failed to recognise the significance of the observation. It was reserved for Arlt (1854) to re-state the problem, and since his time the relationship of ordinary myopia to axial lengthening of the eye has received general recognition. Donders (1866), by ophthalmometric measurements, showed that in the majority of cases the cornea of the myopic eye was even flatter than normal, so that the myopia "is almost entirely dependent upon a lengthening of the optic axis due to staphyloma posticum."

Donders, on clinical grounds, divided myopia into stationary, tem-

porarily progressive, and continuously progressive forms, a classification which was generally adopted. Stationary myopia comprises low degrees which show little or no tendency to increase. Temporarily progressive myopia is characterised by gradual increase up to about 7—9 dioptres, ceasing at about puberty. Continuously progressive myopia shows no tendency to reach its limit until the third or fourth decade or later.

The chief changes in the fundus of the myopic eye, seen ophthalmoscopically, are : (1) the " myopic " crescent or conus ; (2) apparent or real change in the form of the disc, with or without nasal supertraction of the retina ; (3) changes at and about the macula ; (4) sharply defined ectasia of the posterior pole—true posterior staphyloma—shown by the presence of a shadow and by the course of the vessels ; (5) Weiss' reflex streak.

The myopic crescent, which is usually situated on the temporal side of the disc, varies in breadth and in appearance. It is generally white, with a sharp edge, often pigmented, towards the normal fundus. In many cases only the part near the disc is white, the peripheral part being yellow or brownish red with choroidal vessels visible upon it. The crescent may be very narrow or one to two papilla diameters in breadth ; in the latter case it extends farther round the disc and may form a ring. In some cases the floor is demonstrably below the level of the surrounding fundus, and for these the term "conus" might be reserved, though there is probably no fundamental difference in nature or structure. The crescent was early, and is often now, included in the term "posterior staphyloma"; this name should be reserved, however, for the ectasia of the posterior pole, of which the crescent is usually, though perhaps not necessarily, a concomitant.

The crescent is by no means confined to myopic eyes, though it is far more common in them than in emmetropic or hypermetropic ; it was described in the latter by Seggel. Donders found it almost without exception from 16 to 20 years of age in myopia of 6—8 D, but rarely in very young individuals. Jäger observed characteristic coni in some new-born children, and Mauthner saw large crescents in children three years old. Stellwag, in 220 cases of myopia of 6—20 D, found absence of the crescent in 21 ; similar statistics by Seggel give a smaller proportion, and he attributes the myopia in these cases to increased corneal curvature. Mauthner differs from these observers in saying that the crescent is absent much more frequently, even in high myopia, and Schmidt-Rimpler, from investigation of school children, concludes that whilst the frequency and size of coni increase with the degree of myopia, they are absent in 20 per cent. of cases with as much as − 6 D. Schleich, in 1026 cases, found no crescent in 18 per cent., it was narrow in 42 per cent., broad in 22·4 per cent., and annular in 9·5 per cent. Whilst Schmidt-Rimpler's statement is true in the main, there is no inevitable relationship between the degree of myopia and the size of the crescent ; cases of high myopia with only a narrow crescent are not very uncommon. Schnabel, in 135 cases with coni, found 99 myopic, 18 emmetropic, and 18 hypermetropic. Hertel gives the following statistics :

Position.	Number of cases.	Per cent. of all conus cases.	Per cent. of all myopes.
Temporal	4598 .	79 .	69
Annular	642 .	11 .	9·6
Inferior	349 .	6 .	5
Superior and supero-internal . .	233 .	4 .	3·5

Per cent.

In myopia of   1— 5 D the crescent was absent in 15·5 of all myopes.
,,   6— 8 D   ,,   ,,   9·8   ,,
,,   9—16 D   ,,   ,,   3·5   ,,

Corresponding statistics from E. Bock are :

Per cent.

In myopia of   6— 9 D the crescent was absent in 36·96 of all myopes.
,,   9—12 D   ,,   ,,   17·2   ,,
,,   12—20 D   ,,   ,,   11·5   ,,

Supertraction of the retina was first described by Jäger in 1861 : he noticed in a highly myopic eye a faintly pigmented crescent on the nasal side.

Changes at and around the macula in high myopia are common, consisting of yellowish, white, or pigmented spots, and not infrequently white branched lines ; diffuse depigmentation and minute hæmorrhages are also found. The spots coalesce, forming irregular areas which may extend to the disc. These changes are usually described as myopic choroiditis, though there is no evidence, clinical or pathological, that inflammation plays any part in the process, and they should be considered atrophic. Small foci of choroidal atrophy also occur at the periphery in some cases, comprising one form of so-called anterior choroiditis. The " hæmorrhages " which have been described are probably tufts of dilated choroidal capillaries. They show little or no change during prolonged observation.

A less common change at the macula is the development of a central circular black spot, first described by Förster (1862), anatomically examined by Lehmus (1875). It has recently been discussed by Fuchs (1901).

These, and less pronounced changes which doubtless occur at the macula, account for the diminution of central visual acuity which may be found in low degrees of myopia and is invariable in the higher grades (cf. Leininberg, Schleich). The choroidal changes vary directly with the amount of myopia, but are more common in the female sex (Hertel).

The ophthalmoscopic appearances of posterior staphyloma in the proper and narrower sense of scleral ectasia were known to v. Graefe, and were described by him as staphyloma verum. They received little attention until resuscitated by Weiss and Masselon in 1891. The observations were elaborated by Caspar and Otto, the latter giving good drawings. He found the condition 55 times among 355 myopic eyes ; it is characterised by fine dark crescentic lines, caused by shadows ; the lines are concentric with the disc, and at them the retinal vessels make sharp bends, or may disappear entirely as at the edge of a glaucoma

cup. The parts of the fundus central to the lines have a distinctly higher refraction than the peripheral parts, showing that they are at a

FIG. 656.

FIG. 657.

FIGS. 656 AND 657.—MYOPIA, WITH STAPHYLOMA POSTICUM VERUM (WEISS).
Knaggs, T. O. S., xxii. Right and left eyes.

more posterior level; they are also paler, partly by contrast, partly by rarefaction of pigment, so that they may be almost albinotic, and show the choroidal vessels. The crescentic lines are usually limited to the nasal

side but may form a circle round the disc. They may be absent even in the presence of well-marked ectasia. Otto found the shadow present in all cases of myopia of 20 D and upwards, and nearly always in cases of 15—20 D. It was found in half the cases of − 11 D to − 11·5 D; in 24 cases of − 9 D it was present 9 times; it was occasionally found in slight but definite degree with − 7 D. Otto found indirect evidence of posterior ectasia between − 6 D and − 9 D. Other observers have noted the condition much less frequently (Weiss, Casper —̣ 4 times in 242 eyes, Knaggs); Masselon found it fairly often in high myopia.

Weiss in 1885 described a fine, brilliant, crescentic "reflex streak" as one of the earliest ophthalmoscopic evidences of commencing myopia: he attributed it to slight detachment of the vitreous, with collection of fluid before the disc. The occasional presence of the streak in emme-
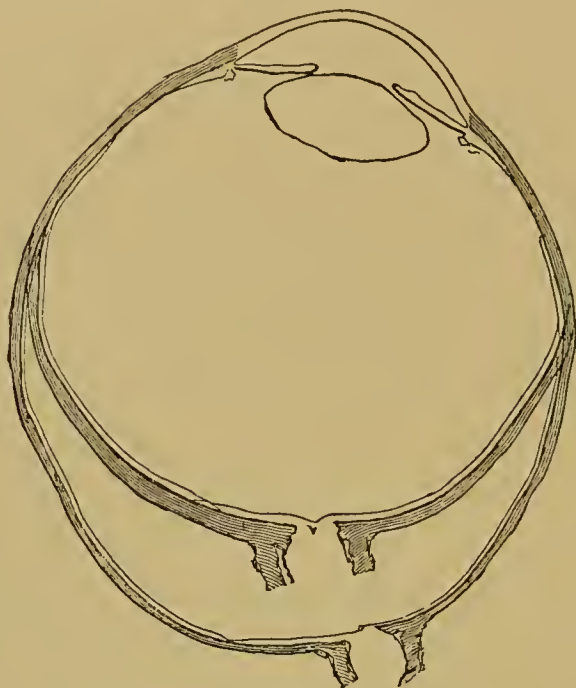
FIG. 658.—EMMETROPIA AND MYOPIA.

Heine, A. f. A., xxxviii. Sections of emmetropic and myopic eyes from same patient superposed, showing identity of pre-equatorial regions.

tropic or hypermetropic eyes is explained by an earlier condition of more marked hypermetropia.

The anatomical investigation of myopic eyes has confirmed the clinical observation that the major changes are found in the posterior segment. This fact is brought out forcibly by Heine, who, by superposition of a section of an emmetropic eye upon a section of the opposite myopic (− 15 D) eye of the same person, showed that the parts anterior to the equators were practically identical (Fig. 658). The only important difference which has been described is in the condition of the ciliary muscle. Arlt found it markedly thicker than in the emmetropic eye. Donders described the origin of the muscle as being more posterior than normal, whilst it was longer, flatter, and more or less atropic. Iwanoff found the muscle thicker and longer than normal; it consisted

almost entirely of meridional fibres (Brücke's muscle), the circular fibres (Müller's muscle) being nearly or completely absent. This condition has been attributed to a disuse atrophy, on the theory that the annular fibres are most used in accommodation, and are therefore hypertrophied in hypermetropia. It has been held that the absence of atrophy of Müller's muscle in some myopic eyes is due to anisometropia and equal accommodation in the two eyes, the myopic eye having to accommodate *pari passu* with the less myopic. Stilling and Hess, the latter in an eye with 20 D of myopia, give examples of typical "hypermetropic" development of Müller's muscle in myopic eyes. Heine confirms the fact pointed out by Iwanoff that the thickest part of the belly of the ciliary muscle is situated more posterior than in the emmetropic, and still more posterior than in the hypermetropic eye, also that there is reduction in volume. It is noteworthy that Merkel and Kallius, E. Fick, and Lange observed marked individual variations in the size and arrangement of the ciliary muscle in new-born children. Lange lays stress on the effect of these variations upon the development and configuration of the globe.

The cornea is probably flatter in axial myopia than in emmetropia, a fact which tends to counteract the effect of the increased length of the eye (*see* " Curvature Myopia ").

The anterior chamber is deeper in the myopic than in the emmetropic or *à fortiori* the hypermetropic eye. This is attributable, *inter alia*, to the ill-developed condition of the ciliary muscle, which entails thinning of the whole ciliary body. It must not be forgotten, however, that the hypermetropic eye is often small in its anterior segment, as shown by the diameter of the cornea (*see* " Glaucoma ").

The greater diameter of the pupil in myopic eyes is attributable in part to the anatomical configuration, in part to the optical conditions. Probably there are other factors of which we are at present ignorant.

Myopic eyes often display opacities in the vitreous, especially in the anterior region. These are explained, though not altogether satisfactorily, by the disturbances in the choroid, which, as has been already pointed out, are not limited to the posterior segment. Vitreous opacities are commoner in women than in men (Hertel), and increase rapidly with age (Ott, Schlesinger, Guttmann, Hertel).

More important are the anatomical conditions in the posterior segment of the eye. In the earlier observations " giant " globes are described (*e. g.* by Donders), characterised by general and uniform distension and thinning of the walls. These are not typical myopic eyes, though doubtless they were optically myopic; they were probably cases of buphthalmia, as is, indeed, indicated by Donders. Durr and Schlegtendal found uniform thinning of the sclerotic in buphthalmia, and these results have been contrasted with the condition found in the typical axially myopic eye by Baas, Maschke, Heine, Schnabel, and Herrnheiser. Whereas in the normal eye the sclerotic steadily increases in thickness from the equator backwards, the myopic eye is thinnest posteriorly, so that it may be one third to one fourth the normal thickness at the posterior pole (Baas), or even as thin as 0·11 mm. The typical configuration of the moderately myopic eye is egg-shaped. The stretching of the walls is not always uniform, and the nasal side may be

more stretched than the temporal, as in many cases of high myopia with sharply defined ectasia (Weiss). Heine considers that the posterior pole is often thinner than is accounted for by mechanical distension, atrophic processes playing a part.

The changes at the posterior pole comprised under the general term "posterior staphyloma," which was used to include the myopic conus, were attributed by v. Graefe to "sclerotico-choroiditis posterior," though he himself subsequently modified his views. v. Jäger and Schweigger pointed out the impossibility of attributing the crescent to inflammatory changes. Donders agreed with this conclusion, but held that the stretching of the coats led to secondary irritative and inflammatory changes; stretching causes stasis in the capillaries of the choriocapillaris, atrophy follows and gives rise to the atrophic crescent.
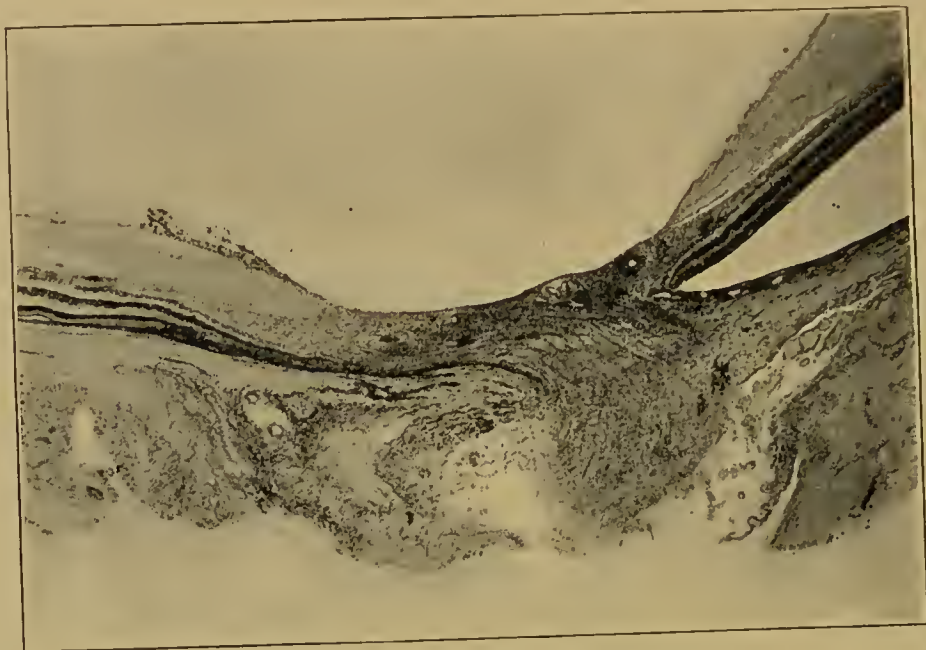
FIG. 659.—MYOPIC DISC AND CRESCENT.
From a photograph by Coats.

Schnabel first drew a sharp line of distinction between the crescent and the ectatic posterior staphyloma proper. He pointed out that many so-called coni are congenital formations; in later writings he is inclined to regard all coni as of congenital origin, a view in which he is supported on anatomical grounds by Elschnig (see "Coloboma of the Optic Nerve"). Hence, from this point of view, the crescent is wholly independent of stretching of the coats of the eye, and is due to non-development of the choroid. This entails an abnormal disposition of the optic nerve head, so that not only is the choroid absent at the site of the crescent, but also the posterior layers of the retina and the pigment epithelium.

Weiss first gave an exhaustive description of the microscopical features of the crescent, derived from the examination of an eye with 5 D of myopia. The supertraction which had been previously observed

ophthalmoscopically was found to be due to dragging of the retina and choroid over the nasal side of the disc. Similarly the crescent showed a dragging of the optic nerve over the temporal edge of the scleral ring.

FIG. 660.
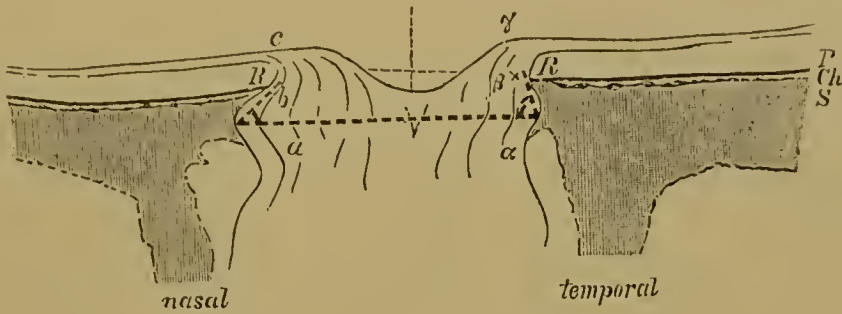
FIG. 661.
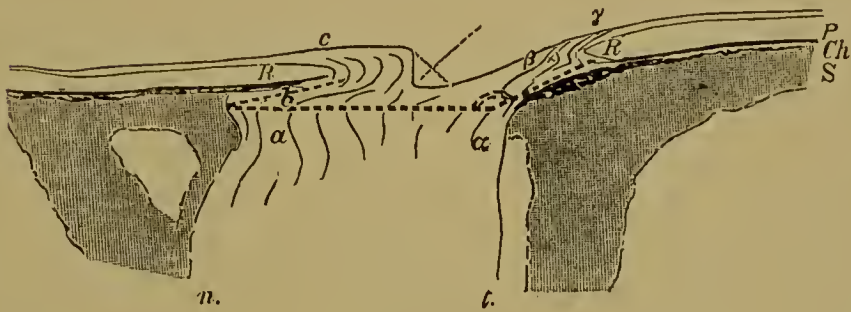
FIG. 662.
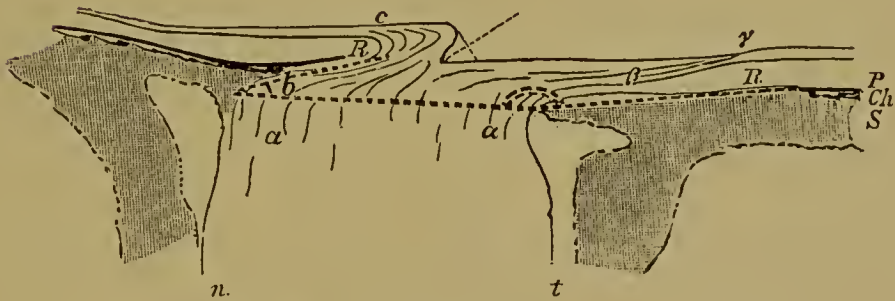
FIGS. 660, 661, AND 662.—EMMETROPIC AND MYOPIC DISCS.

Heine, A. f. A., xxxviii. Fig. 660.—Emmetropia. Fig. 661.—Myopia of 10 D. Fig. 662.—Myopia of 15 D. The horizontal line corresponds with the lamina cribrosa. In the emmetropic eye the nerve-fibres on the nasal side make a bend, convex towards the nasal side, from a to b, then another bend, concave towards the nasal side, from b to c. In the myopic eyes the bend from b to c is rectangular or even acute, owing to the supertraction of the retina and choroid towards the temporal side. In Fig. 662 the pigment epithelium reaches almost to the axis of the nerve on the nasal side, whilst on the temporal side it fails to reach the nerve by a considerable distance.

These results are confirmed by the simultaneous observations of Duke Carl Theodor, and by the subsequent researches of Schnabel, Herrnheiser, Heine, and others. Weiss also drew attention to the widening

of the intervaginal space in its whole circumference; in one case the space reached so far forwards that only a few layers of scleral lamellæ persisted.

The ophthalmoscopic observation of supertraction by Jäger was substantiated by microscopic investigation, and, as has been mentioned, was confirmed by Weiss. Nagel drew attention to the frequency of small degrees of supertraction in early cases of myopia. In high myopia he found that the retina might be dragged almost to the centre of the disc, but that the choroid appeared to lag behind, this being due to subsequent atrophy. Heine demonstrated the dragging outwards of both retina and choroid, though the choroid seems to be always less displaced than the retina.

Stilling propounded an ingenious explanation for the conus. According to him the lateral dragging upon the papilla manifests itself most upon the temporal side. The normal scleral canal is conical, with the smaller aperture anterior. The canal in myopia is cylindrical but oblique, so that seen in front it appears triangular or conical in perspective. The position of the conus is conditioned by the direction of the tendon of the superior oblique, a suggestion which reveals the influence of Stilling's theory of myopia (v. infra) upon his interpretation. That the perspective appearance of the scleral canal is a factor in the production of the ophthalmoscopic picture of a myopic crescent must be accepted in some cases, but fails to explain the majority, especially those in which pigment patches are seen. Anatomical observations of cases in which remnants of the choroid are found in the area of the crescent have been given by Elschnig and Heine.

The mode of ending of the intervaginal space of the optic nerve is notoriously inconstant. It usually ends in a point between the pia and the sclerotic, as first shown by v. Jäger, jnr., and is separated from the choroid by only a thin layer of sclera. v. Michel showed that the end was often dilated, being triangular in section when the dura passes obliquely into the sclerotic. The cleft is pulled out laterally in most myopic eyes, but the same condition may be seen in emmetropic eyes. The intervaginal space usually extends farther forwards on the temporal than on the nasal side.

The investigations of Schnabel and Herrnheiser and of Elschnig tend to show that transition forms between the normal connective-tissue ring around the disc and the fully-developed crescent occur. According to Elschnig there are three types of connective-tissue ring: (1) the commonest form, in which the limiting tissue (v. Vol. II, p. 656) is covered by the membrane of Bruch, which, however, carries no pigment epithelium, or only degenerate remnants; (2) in which the choroid ends flush with the sclera, the limiting tissue consisting of parallel fibres resembling choroid, but uncovered by lamina elastica or pigment epithelium; (3) in which the lamina elastica, covered by normal epithelium, ends outside the optic canal, so that the rounded edge of the sclera and choroid, clothed with more or less limiting tissue, lies exposed on the inner surface. What Elschnig calls limiting tissue, which he has shown to be a normal structure, most writers on the myopic crescent have confounded with atrophic choroid. Only a thorough

knowledge of the variations which may occur in emmetropic eyes permits of accurate differentiation. It would seem that either of Elschnig's types of connective-tissue ring may give rise to conus, but the third form is commonest in myopia; the second is rare, giving rise to annular conus, as shown by a case of Schnabel and Herrnheiser.

It is difficult to conceive how mere increase of stretching can produce an annular conus, entirely surrounding the disc. Schnabel definitely states that the transition from the ordinary temporal crescent to the ring conus does not occur, and Salzmann agrees that the latter is due to the fusion of atrophic areas in the choroid and retina, these being most frequent in the neighbourhood of the papilla (v. infra). It is possible that the slighter, more regular, ring conus is an exaggeration of the normal scleral ring.

Heine lays chief stress upon the lamina elastica of Bruch in the production of the conus, since it does not yield to stretching in the same degree as the retina, choroid, and sclerotic. Hess concludes a review of the anatomical observations by stating that the ophthalmoscopic picture of the conus is caused essentially by the pigment epithelium stopping short at some distance from the disc, so that the parts lying posteriorly become directly visible. If the choroid fails here completely, then the inner surface of the sclerotic, or in some cases the inner wall of the scleral canal, is seen, the conus appearing white. If, however, more or less choroidal tissue persists, the conus looks yellowish red or brown, and is often traversed by choroidal vessels.

Schnabel and Herrnheiser differ from most ophthalmologists in their opinion that the crescent is of congenital origin, the prevalent view being that it is an expression of stretching of the walls of the globe. According to Elschnig in the 6—7 months foetus the limiting tissue fills a cleft between the edge of the disc and the innermost layers of pia. This mass of tissue forms the junction between the choroid and the disc, and may persist, a condition which Elschnig considers a true coloboma.

Increasing evidence tends to support the congenital theory, though it is impossible to deny the effect of posterior staphyloma in causing enlargement of the crescent (distraction crescent, Dimmer). On the other hand, the ectasia itself is most reasonably accounted for on the theory of an inherent congenital weakness of the sclerotic (v. infra). At the same time the two abnormalities must be kept severely distinct. If the conus is congenital, it is the minimal expression of an atypical coloboma (q.v.), whereas there is at present no reason to suppose that the posterior staphyloma has anything in common with a coloboma.

As already pointed out, posterior staphyloma is characterised by ectasia, with thinning of the sclerotic in the posterior part of the eye. The lamellæ are reduced in number and compressed. It has been stated that elastic fibres are deficient (Lange), but this has been disproved by Hosch and Elschnig. The difference in level of various parts of the staphyloma verum as observed ophthalmoscopically by Weiss and others is confirmed by anatomical investigation.

It is obvious that the retina and choroid must be greatly stretched in cases of large posterior staphyloma. It has been estimated that the

area of the fundus posterior to the equator in the normal eye measures about 9 square centimetres; this is increased by 4–6 square centimetres in an eye 31 mm. in length. The relatively inelastic retina must inevitably be disordered by the stretching, which, however, is generally unevenly distributed. Anatomical evidence of gross lesion may be absent; for example, the pigment epithelium may be quite normal in an eye with 12 D of myopia (Heine): such signs of tension as obtain are more manifest in the inner than in the outer layers. Donders attributed the lower vision in myopia to the stress and strain on the retina, and Mauthner held that the defect in acuity both in myopia and hypermetropia was due to disordered function in the cones. Knapp's statement, that the cones are thicker at the fovea in hypermetropic and thinner in myopic eyes, rests upon theoretical considerations, and has been substantiated by no exact observations. The changes found at the macula, so often seen ophthalmoscopically, are essentially retinal, the choroid being little involved (Heine). It may be thinned, but shows no hyperæmia, infiltration, or scarring. The membrane of Bruch may be unusually thin, and is sometimes broken and split (Salzmann). The foveal depression in the retina passes more gradually than normal into the surrounding part. The most pronounced changes are seen in the pigment epithelium, which is clumped into three or four layers, and deeply pigmented in parts, whilst the pigment is rarefied in other parts. In places the epithelium is absent; elsewhere layers of spindle-shaped cells resembling smooth muscle-fibres are found. The cones show a tendency to degenerate *pari passu* with the epithelium, the outer limbs becoming smaller, whilst groups of cones fuse and atrophy, so that they may disappear over considerable areas.

In the black spot which occasionally occurs at the macula Lehmus found that the densely pigmented retinal epithelium was clumped together, so that it might attain a thickness equal to two thirds that of the choroid. There was a gelatinous, non-cellular exudate, possibly fibrinous, upon the surface of the epithelium, and the retina was adherent.

Much attention has been directed to the size of the blind spot in myopia, enlargement of which might be anticipated in the presence of conus. v. Graefe found that this occurred in only relatively few cases. Donders showed that perception of light was not absent over a narrow crescent, but that it was completely or almost completely abolished in higher grades (*cf.* Marsikani and Woinow, Schnabel, Mauthner). Lateral displacement of the blind spot, corresponding with the super-traction of the retina on the one hand and the crescent on the other, might be anticipated, for anatomical observations point to the fact that the percipient elements reach only as far as the pigment epithelium. Hence, the distance between the fovea and the centre of the blind spot becomes of interest. Landolt, Dobrowolsky and Volpe found this diminished in myopia and increased in hypermetropia, as compared with the normal 4—5 mm. of the emmetropic eye. Mauthner was unable to find any difference in myopia of 3—7 D. It must be remembered that the determination by the perimeter demands the consideration of several factors—*e.g.* the increased distance behind the posterior nodal

point of the eye, in addition to the mere stretching of the sclera, which is again complicated by the oblique direction of the retina between the disc and fovea. In Heine's preparations anatomical measurement showed that the distance was definitely increased in myopic eyes, whilst the distance between the fovea and the edge of the pigment epithelium was normal. In the new-born the fovea is as far from the centre of the papilla as in adults, the temporal side of the fundus being relatively larger than the nasal (Merkel and Orr)—i. e. during growth the nasal part grows proportionately to the general growth, whilst the temporal part, which is early more advanced, lags behind (Elschnig).

Contraction of the fields for white and colours, as well as crescentic or ring scotomata have been observed by Weiss, Otto, and Wettendorfer.

The condition of the choroid in the grosser changes of myopia is one of stretching and atrophy, with little or no evidence of inflammation.
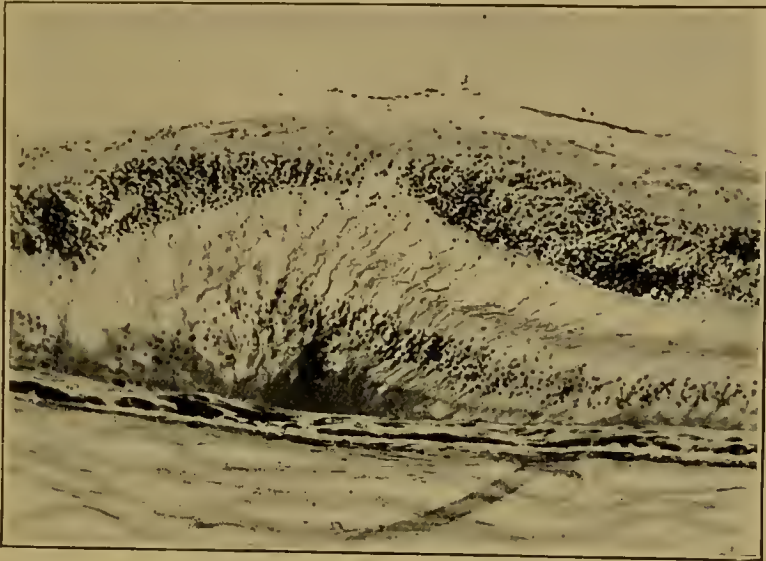
FIG. 663.—MYOPIA.
From a specimen by Coats, showing changes at the macula.

Salzmann found defects in the lamina elastica in the affected areas; they appeared as clefts, or branching or reticular figures when reconstructed from serial sections. Near the papilla they are mostly concentric with it; they are attributed to stretching. The tears lead to proliferation of the pigment epithelium and cicatrisation, differing in no way from the scarring following choroiditis; hence the great similarity in the ophthalmoscopic appearances. The scars themselves lead to fresh tears owing to their resistance and lack of elasticity, so that the changes are progressive. The chief change in the choroid itself is the disappearance of the lumina of the vessels. Large vessels are seen, but they merely traverse the atrophic areas; the smaller vessels and capillaries fail completely. It is true that when the choriocapillaris remains intact in myopic eyes it usually contains leucocytes, which are normally absent; this is evidence of the irritative effect of stretching rather than a definite sign of inflammation, According to Schweigger the chromato-

phores first lose their pigment, then disappear, and this is followed by atrophy of the choriocapillaris and consequent degeneration of the pigment epithelium. Finally the larger vessels become obliterated, and last of all the elastic elements disappear.

The retinal changes are wholly secondary to those in the choroid. They are at first limited to the outer layers, which are dependent upon the choriocapillaris for their nutrition. Failure of the blood-supply in this layer causes the same changes which have already been described in treating of retinitis pigmentosa (q. v.), choroiditis (q. v.), etc. The neural epithelium suffers with the degeneration of the pigment epithelium. The atrophy ceases usually with the outer reticular layer, the inner layers of the retina receiving their nutrient supply from the retinal vascular system. Fusion with the choroid occurs where the lamina elastica is defective, as in disseminated choroiditis. The degeneration at the macula may go on to the formation of an actual hole (Coats) (Fig. 664).

The atrophic patches occur anywhere in the staphylomatous area,

FIG. 664.—HOLE AT MACULA.
From a specimen by Coats.

but show a predilection for the circumpapillary zone, where they may fuse with the crescent. This fusion with the crescent appears more complete ophthalmoscopically than it really is, as shown by microscopical examination.

Salzmann holds that the ruptures in Bruch's membrane are spontaneous (cf. Schwersenski, de Wecker and Masselon) and primary—i. e. they are not due to atrophy of the choriocapillaris. The stretching of the choroid is passive, merely following the bulging of the insufficiently resistant sclerotic.

Detachment of the vitreous in myopia was asseverated by Iwanoff, the space being filled with fluid exudate. This was held to be the cause of the reflex streak by Weiss, but Elschnig denies that it occurs (v. Vol. II, p. 431).

Detachment of the retina occurs in the higher grades of myopia. Hertel observed it in 0·96 per cent. of all cases of myopia; Proskauer found it in 0·71 per cent., Schleich in 2·3 per cent. Higher percentages given by Ott, Schlesinger, Guttmann, and A. v. Hippel refer only to

cases over − 6 D or − 10 D. It occurs more commonly in women, and is more frequent the older the patient, being rare before 30 and showing a considerable rise above 50 years (Poncet, Nordenson, A. v. Hippel, Hertel). There is some relationship to the degree of myopia; it occurs in all grades, but especially above 13 D. It is about four times as common in myopes as in non-myopes (Hertel); in Nordenson's cases 60 per cent. were myopes. Hertel observed greater frequency of detachment of the retina in peasants and manual labourers than in other classes quite apart from the refraction. It is outside the scope of this work to consider the relationship of retinal detachment to operative interference in myopia (*cf.* Voigt).

Myopia is rare in the new-born; the early observation of Jäger (1861), that 78 per cent. are myopic, has been disproved. Ely found only 2 per cent. if atropin was used, Horstmann 10 per cent., Bjerrum 34 per cent.; later investigators—*e. g.* Königstein, Ulrich, Schleich, Herrnheiser—found no case of myopia among about 3200 eyes. Horner noticed abnormally long eyes, but the discs were cupped, so that
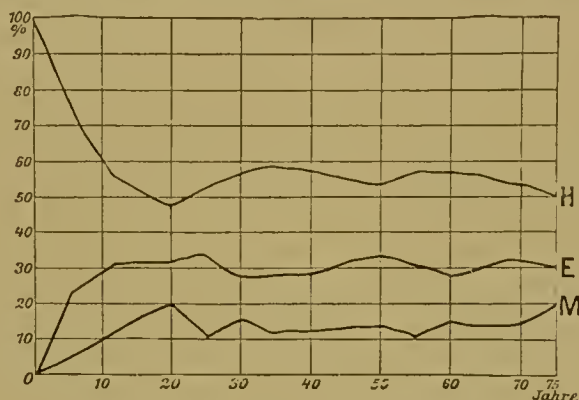
FIG. 665.—AGE-INCIDENCE OF MYOPIA, etc.
After Herrnheiser—Ordinates, percentages; abscissæ, ages.

they were really cases of buphthalmia. The corneal curvature is greater in the new-born than in adults, measurements showing a radius of 6·59—7·138 mm. (v. Reuss), 6·75—8·1 mm. (Laqueur) 6·06 mm. (Hasner), 7—7·44 mm. (Axenfeld); this corresponds with a higher refraction of 4—5 D, which demands for its counteraction and the usual hypermetropic refraction of the new-born, of a stronger action of the lens, equivalent to 25—30 D (Hess). The shallowness of the anterior chamber also tends to a myopic refraction. The spherical shape of the lens, with a radius of 3·3 mm. (Merkel and Orr), a thickness of 5·1 mm., and an equatorial diameter of 6·5 mm., suffices to account for the total refraction found.

The percentage of myopes increases rapidly during the first two decades of life, as is shown by statistics, derived from over 11,000 eyes by Herrnheiser (Fig. 665), 12,331 patients by Hertel, etc. Thence onwards it remains at about 10—15 per cent., as compared with 30 per cent. for emmetropia and 50—55 per cent. for hypermetropia. The percentage curve for myopia shows a slight rise in the eighth decade, attributable to lenticular myopia (*v. infra*). Randall's very exhaustive

researches on over 200,000 eyes confirm these results. He found myopia almost unknown before the school period, and then only in the higher classes, especially in German schools, thus—small children 2·2 per cent., in 488 eyes of children before the commencement of schooling, 6·5 per cent.; in 23,315 eyes, during the first three school years, 6·8 per cent.; in 3052 eyes of young persons, 11·4 per cent.

As regards sex, there is no doubt that the higher grades are commoner in women (Schleich, Horstmann, Tscherning, Hertel). Schweitzer observed macular changes twice as often in women. Proskauer, in myopia of 9 D and over, found 10 per cent. men to 14 per cent. women, in the lower classes, whilst in the middle classes engaged much in near work more men than women were affected. Leininberg found both the relative and the absolute numbers of female myopes less than that of males. Widmark observed far more men than women with myopia up to 4 D, whereas at 5 D the number of women was greater, and in the higher grades it was very much greater. In schools he noticed a greater tendency to myopia in girls than boys. Pflüger gives similar results for Switzerland, and Bjerrum for Denmark. Knöpfler could distinguish no influence of schooling in the lower classes; the effect of near work was only noticeable after puberty, especially in women, who in this position in life do much more near work than the men. Hertel, from a careful investigation of the cases attending the Jena clinic over a period of 10 years, considers that the female sex is more prone to myopia in all grades than the male.

Few observations seem to have been made upon the racial distribution of myopia. Nicati, in Marseilles, found more in the Jewish than in the Christian schools; most observers have mentioned hypermetropia as more characteristic of the Jews. Stephenson, at the Central Foundation Schools in London, amongst 918 boys and 231 girls, found 10·63 per cent. of the Jews myopic, as compared with 1·97 per cent. of the Christians. The percentage of myopia in Jewish boys was more than six times greater than in Christian boys, and three and a half times more in girls. Myopia is frequent amongst the highly-educated natives of India.

Stilling considered that consanguinity was an important factor in the causation of the worst forms of myopia with fundus changes. Velhagen, who investigated 50 high myopes, whose punctum remotum was at 11 cm. or less, found only one case with consanguinity, though he did not choose the specially deleterious forms. Wolff found 8·75 per cent. in 126 high myopes with fundus changes when consanguinity could be demonstrated, whereas Otto failed to find this factor in the rich material afforded by the Leipzig clinic.

Horner and Stilling drew attention to the ill-nourished and anæmic condition of most high myopes with fundus changes; the latter compared the condition with the passive dilatation of the heart found in chlorotic women.

Kepler first associated short sight with near work, a point repeatedly emphasised by Ware and others. Numerous and exhaustive statistics from this point of view have been collected by Cohn, Randall, and others.

Hertel divides his cases, 7292 in number, into peasants, those engaged in coarse manual labour requiring little close eyework, and students and others engaged in fine work. Amongst the peasants 32·3 per cent. were emmetropic, 46·4 per cent. hypermetropic, 21·3 per cent. myopic; in the second group 33 per cent. were emmetropic, 40·7 per cent. hypermetropic, 26·3 per cent. myopic; in the third group 22·9 per cent. were emmetropic, 25·5 per cent. hypermetropic, 51·6 per cent. myopic.

Donders drew attention to the fact that near work could not be the sole cause, since the highest grades of myopia might be observed amongst people who rarely used their eyes in this manner. Similar considerations led Hoor and others to minimise the effect of near vision, the eyes being congenitally disposed to myopia, so that they would become elongated independently of it.

Near work, whether the *causa causans* or not, is now almost universally admitted to have a deleterious influence, and much discussion has arisen as to the method of its action. Arlt attributed it to repeated temporary increase in pressure in the vitreous chamber. Donders invoked a predisposition to the development of posterior staphyloma, a factor which few—*e. g.* Erismann and Dobrowolsky—have denied. Donders attributed the effect of near work to three chief causes: (1) pressure of the extrinsic muscles upon the globe in strong convergence; (2) increased intra-ocular pressure from vascular congestion, due to the position of the head; (3) congestion of the fundus, leading to softening of the tissues.

That accommodation *per se* could cause myopia was first seriously advocated by Erismann and Dobrowolsky, though Dobrowolsky later attributed the major effect to convergence. Donders, Jäger, and Stellwag considered that it was unlikely that accommodation was the cause. It is at once apparent that myopes of more than 3 D have no necessity to accommodate, whilst emmetropes, and *a fortiori*, hypermetropes accommodate much more. Förster pointed out that the ciliary muscle can act only on the choroid, and cannot exert any effect upon the sclerotic. The favour which the accommodation theory received was largely due to the view that accommodation caused increase of the intra-ocular tension; this has been definitely disproved by Hess and Heine.

Arlt early pointed out that, apart from compression of the vitreous as a whole, contraction of the ciliary muscle could not conceivably produce any change in the shape of the globe. Even the view enunciated by Iwanoff, and supported by Horner and others, that the crescent is directly due to traction of the choroid by the contracting ciliary muscle, cannot be accepted. The same arguments militate against this theory, since crescents should then be common in hypermetropic eyes, and the myopic crescent should not be progressive. Moreover, Hensen and Völckers adduced experimental evidence that the ciliary muscle exerted no traction upon the posterior part of the choroid; needles passed through the walls of the globe behind the equator moved scarcely at all, at the macula not at all, when the ciliary muscle was stimulated to contract, whereas those in front of the equator

showed very obvious movements. Mauthner's suggestion, that accommodation produced hyperæmia of the choroid, and thereby increased tension, is not supported by direct evidence, and is controverted by the conditions found in hypermetropia. The same author strongly supports the view that commencing stretching of the choroid leads to spasm of the ciliary muscle. The latter has often been stated to be of common occurrence in myopia, but upon quite insufficient grounds. It has been thought to cause more or less permanent increase in curvature of the lens (Jäger), but direct measurements, though scanty, are against the theory.

The mechanism whereby convergence influences the production of myopia receives different explanations by various authors. Most agree that the pressure of certain extrinsic muscles causes increased intra-ocular tension. Arlt considers that the pressure impedes the outflow of blood by the vortex veins, so that congestion results. He regards the external rectus and inferior oblique as the offending muscles. Philipp (1840) and Stilling impeach the superior oblique. Most other authors consider that the external and internal recti are responsible. A. v. Graefe's support of the convergence theory led to a series of therapeutic and prophylactic tenotomies of the external recti, and Gerloff went so far as to recommend tenotomy of both external and internal recti.

There is no doubt that the action of the extrinsic muscles causes increased intra-ocular tension, a fact which is readily proved experimentally, and makes the use of curare imperative in manometric observations upon the tension. Even if the tension is normally greater in myopic eyes (Arlt, Mackenzie, Donders, Hasner, Junge), which is certainly not proved, the effects of increased tension on young eyes is quite different from the condition found in myopia (see " Buphthalmia "). Arlt and Stilling consider this to be due to the increase not being continuous, and to its low degree.

It is obvious that neither accommodation nor convergence can alone suffice to explain the genesis of myopia. There must be some individual predisposition which provides any such accessory causes with advantageous conditions. This has been sought by various authors in the eye itself, or in neighbouring parts. Of the latter group the shape of the skull or of the orbit and the length of the optic nerve have received most attention.

Mannhardt, agreeing with v. Graefe in attributing the major importance of convergence to the external recti, concluded that the effect would be increased by unusually great distance between the eyes. Measurements of interpupillary distance, though discordant, fail to reveal any definite relationship with refraction. In any case the differences are very slight. Thus, Pflüger found that hypermetropes had narrow skulls. Schneller found the mean interpupillary distance in hypermetropes 59·95 mm., in emmetropes 59·9 mm., in myopes 61·45 mm. Koppe and Adamück support Mannhardt's theory, Horner and Mauthner reject it. Emmert, Beselin, and others found the difference too slight to be of importance. Amadei and Bono noted some relationship of hypermetropia with brachycephaly, and of myopia with

dolichocephaly. Erismann found the interpupillary distance 0·2—0·3 mm. greater and Bjeloff smaller than in emmetropia. Seggel found the distance between the centres of rotation in myopes from 10 to 12 years of age less than, from 13—17 equal to, above 18 greater than, that in emmetropes.

Stilling's theory is that the lengthening of the eyeball is due to pressure of the superior oblique, and that this varies with the position of the pulley of the muscle, and hence depends upon the configuration of the orbit. Thus, if the pulley is below the normal level much compression is exerted, and Stilling's measurements tend to show that the orbit is broad and low in myopes, a condition which he calls chamæchonchy, as opposed to the hypisconchy of hypermetropes and emmetropes. The broad orbit is merely one feature of a broad skull and face—chamæprosopy, the narrow and high orbit corresponding with a narrow face—leptoprosopy. Stilling and his pupils Cohen, Romano Catania, Krotoschin, and others have made many measurements to determine the mean orbital index—i. e. 100 times the height divided by the breadth. Stilling's value for emmetropia is 89·1, for myopia 77·8. Most other observers have failed to obtain confirmatory evidence (Baer, Schmidt-Rimpler, Seggel, Herrnheiser, Weiss). Schmidt-Rimpler found the orbital index in 1300 cases equal to 94·4 for emmetropia and hypermetropia, and 94·5 for myopia, and Weiss obtained similar results. Seggel found the orbit 2 mm. lower in young myopes than in emmetropes of the same age, and 3 mm. lower than in hypermetropes : they were mostly boys, who generally have a lower orbit than girls. Kirchner supports the improbable suggestion of Schmidt-Rimpler that such difference as exists is the result, not the cause, of the myopia, and is due to the traction of the obliques upon the upper and lower orbital walls. Weiss and Herrnheiser failed to observe any difference between the two orbits in anisometropia.

Février (1896) advanced a totally different theory of myopia, also dependent upon the action of the obliques. He suggested that during development the vertical meridians of the retina were unsymmetrical; the obliques endeavour to establish parallelism, thereby inducing lengthening and protrusion.

The theory that myopia is due to the optic nerve being too short, either absolutely or relatively, originates in Hasner's conjecture that the conus is due to this cause. The theory was supported by Emmett and Paulsen, and has been elaborated by Weiss. The latter terms the difference between the length of the nerve and the distance from the optic foramen and the back of the sclerotic the rotation segment. It varies greatly, so that two groups of aberrant cases may be distinguished, viz. those in which it is more than 7 mm. and those in which it is less than 5·5 mm., with a mean amongst the latter of 4·46 mm. Weiss concludes that when the nerve is abnormally short the papilla is pulled upon and "the ground is prepared for ectasis." Stilling found the condition extremely seldom in 200 *post-mortem* examinations, and then in otherwise normal eyes. Further, traction effects were seen with the longest rotation segments and might be absent with the shortest. Schnabel considers that shortness of the nerve will not explain the

conditions described by Weiss himself, and Hess cannot accept the view that it will produce general ectasia of the posterior wall of the eye, which may be involved as far forwards as the equator.

The evidence in the matter of the extrinsic theories of myopia is therefore discordant and unsatisfactory. More weight must be attached to what may be called the intrinsic theories. Mauthner voices the general opinion when he states that " the congenital basis of myopia is to be sought in nothing else than in a defective resistance of the sclerotic, especially in its posterior half." This view has been adopted particularly by Schnabel and Herrnheiser, who have attempted to bring forward anatomical evidence in its favour. If an emmetropic eye is placed upon the table with the cornea downwards, it retains its shape ; if, however, a myopic eye is similarly placed, even though it differ little in shape from the emmetropic, some part of the posterior wall in the neighbourhood of the nerve will sink inwards. Thus Weiss found that in an eye with moderate myopia an oval area of the sclerotic, 17 mm. by 12·5 mm., became depressed, the nerve-entrance being situated in the nasal part of the oval. Changes are always to be observed at the posterior pole, though they vary much in degree. They are especially noticeable around the disc, and may be limited to the choroid in the form of a crescent, or may involve the sclera, though usually both participate. The opponents of the theory naturally consider the changes to be the results of the myopia, and it is impossible in many, perhaps most, cases to apportion them definitely. We are dealing, in fact, with a vicious circle.

Whether in addition to a congenital weakness an acquired factor must also be invoked is uncertain. v. Graefe enunciated the view that the changes at the posterior pole were the outcome of a sclero-choroiditis, but he himself modified his opinion on finding no anatomical evidence of inflammation. Later observers agree that inflammatory stigmata are usually absent, Heine's careful researches being especially noteworthy ; he found the degenerated retina sharply delimited by an intact lamina vitrea from the normal, though much stretched choroid and sclerotic. At the same time it must be remembered that there is little or no difference between the ultimate effects of inflammatory lesions and the condition found in myopia, and that a very slight chronic inflammation may present few objective microscopical features. It may be that the lower grades of myopia are entirely congenital in origin, whilst the higher grades of so-called progressive myopia have in addition ætiologically a true inflammatory factor. Schön points out that scleritis is always accompanied by choroiditis, and that it is not improbable that the converse may occur. It is more probable that in these cases both are due to a common cause (see "Annular Scleritis," Vol. I, p. 273). In this connection there is, again, the difficulty of distinguishing between cause and effect, and Seggel, admitting the presence of sclero-choroiditis posterior, attributes it to myopia.

That choroiditis can in certain cases induce myopia is accepted by many authors (Knies, Tscherning, Nordenson). Ferri considered this to be so when myopia rapidly develops in adults who were previously

emmetropic. Priestley Smith strongly supports the view that severe choroiditis, especially syphilitic, may give rise to rapid and pernicious myopia.

The question whether the well-known clinical varieties of axial myopia differ from each other fundamentally or only in degree has received much attention. Tscherning divides myopia into a benign form, with a mean refraction of 3 D and a maximum of 9 D, and a malignant form of 9 D and more. He considers them fundamentally distinct; in the first group the influence of heredity may be detected. Seggel considered that spasm of accommodation in healthy ancestors might induce a disposition to myopia, manifesting itself in later generations. Such an assumption is contrary to current views of the inheritance of acquired characteristics, and in any case there is no evidence that myopia has increased during the last three or four decades (Becker). Only the second group are subject to dangerous complications, the result, according to Tscherning, of an insidious choroiditis. He doubts whether near work has any influence on the malignant form, basing this conclusion on its infrequency, its relative frequency in the lower classes and in women. The view of Schleich and Tscherning that high myopia is commoner in peasants is opposed by Priestley Smith, Widmark, Proskauer, and others.

Widmark found 1·73 per cent. of myopia of more than 10 D amongst 4000 private patients, as against 0·43 per cent. in 10,000 polyclinic patients. Proskauer found twice as many high myopes amongst those engaged in near work compared with the lower classes.

Stilling further divides high myopia into two groups, an occupation myopia, arising in otherwise healthy eyes as the result of muscular pressure induced by near work, and a deleterious form, with serious complications, the result of a glaucomatous process going on in previously unhealthy eyes. The fundamental independence of deleterious myopia and buphthalmia is proved by anatomical investigation (see " Buphthalmia ").

Schnabel and Herrnheiser strongly maintain the ætiological unity of the myopic process in all forms of axial myopia. They, however, admit a difference in shape of the eye in the medium and high grades, the former approximating that of the emmetropic eye. The staphyloma is not merely a higher degree of the anomaly which causes low and medium myopia, nor are true transition forms between this grade and the higher met with. According to these authors, school myopia never passes into the more serious form; on the other hand, it is impossible to prevent the development of a staphyloma where the predisposition occurs.

The theory of the absolute independence of the medium and high grades of myopia has been opposed especially by Horner, Nordenson, Otto, Schneller, Pflüger, Seggel, and Priestley Smith. These authors doubt the harmlessness of occupation myopia, and bring forward cases to prove that it may be progressive, and further, that detachment of the retina may occur (Nordenson). This serious complication is almost limited to the higher grades, and is even then rare—0·5 per cent. (Fischer), 1·25 per cent. (Fröhlich) : much discussion has arisen as to

whether the tendency to detachment is increased by removal of the lens.

The attempt has been made to explain occupation myopia on teleological grounds as a useful adaptation. Such a theory has little in its favour, since the relief afforded by abolishing three or four dioptres of accommodation in early life is inappreciable, and is purchased at high cost, whereas it never occurs after 45, when it would be most advantageous.

Curvature myopia may be due to increased curvature of the cornea, or of one or both surfaces of the lens.

Corneal curvature myopia is much rarer than axial myopia; nevertheless increased curvature of the cornea not infrequently occurs, since it is not inconsistent with an emmetropic refraction when counteracted by diminished length of the eye. Mauthner calculated that since the radius of the cornea varies from 7 to 8·5 mm. the length of the emmetropic eye must vary from 22·25 to 26·24 mm., and these numbers agree well with actual measurements by Schnabel and Herrnheiser.

The cornea in axial myopia is probably flatter than normal, though actual measurements give discordant results. Donders gives the following mean results: in men, emmetropia (27 eyes) 7·785 mm., myopia (25) 7·874 mm., hypermetropia (26) 7·96 mm.; in women, emmetropia (11) 7·719 mm., myopia (12) 7·867 mm., hypermetropia (15) 7·767 mm. Mauthner found the mean radius smaller in myopia and hypermetropia than in emmetropia, whereas it increased in high hypermetropia and diminished in high myopia. Javal considered that the mean radius was smaller in myopia, basing his opinion on measurements by Nordenson, in which in 452 eyes there were 90 myopic with a mean corneal refraction 1 D higher than in 319 emmetropic, and 63 hypermetropic. Stilling found large radii in myopia up to 2 D, smaller in myopia from 2 to 7 D; these results are opposed to the theory of myopia in otherwise healthy eyes (Landolt, Tscherning). Sulzer examined 1114 eyes with Javal's ophthalmometer, the mean corneal radius being 7·628 mm. He found the cornea in myopia more, in hypermetropia less, curved than in emmetropia. Valk in 1106 eyes found 620 with a radius greater than 7·65 mm., including 57, or 10 per cent., myopes; in 486 cases, with a radius less than 7·65 mm. 110, or 33 per cent., were myopes; these results confirm Sulzer's. Otto in 179 corneæ, measured by Javal's ophthalmometer, found the mean radius in myopia less, in hypermetropia more, than in emmetropia, though the difference amounted to less than 0·2 mm.

Most of the cases of true corneal curvature myopia occur in eyes in which the cornea is diseased (*see* "Conical Cornea," Vol. I, p. 174).

Lenticular curvature myopia has been little investigated; it may be a factor in the myopia of early senile cataract and diabetic cataract (*v. infra*).

v. Reuss found the radius of curvature of the anterior, and usually that of the posterior, surface of the lens much greater in myopes than in emmetropes; the mean anterior radius was 12·69 mm. The lens was thinner than normal. It is possible that, owing to the larger pupil in

myopia, the somewhat flatter periphery of the lens was measured (Hess).

Most cases of lenticular curvature myopia occur in diseased eyes. They include anterior and posterior lenticonus (q. v.) and pathological relaxation or rupture of the suspensory ligament. In sublaxation and ectopia of the lens the curvature will be greater the younger the patient. In a case of ectopia lentis in a child, æt. 7, Hess found the refraction in the aphakic part of the pupil $+10$ D, in the phakic part -15 D. The myopia will be greater if the polar region of the lens is in the pupil than if this is occupied by the flatter periphery. Myopia has been observed in shrinking globes and may be due to relaxation of the zonule (Hess), though it has also been attributed to spasm of accommodation (Nagel, Schmidt-Rimpler). Hess observed a myopia of $+5$ D develop in an eye during iridocyclitis, and acute spontaneous myopia, possibly attributable to uniform relaxation of the suspensory ligament, has been described by Schrötter.

Index myopia may be due to abnormal refractive index of the cornea, aqueous, lens, or vitreous.

Aqueous index myopia is due to increase in the refractive index of the aqueous. Slight myopia of 1—2 D has been attributed to this cause in iritis (Schapringer), jaundice (Moauro), diabetes (Appenzeller), etc. Schapringer's and Moauro's remarks are based upon inaccurate calculations (Hess). The production of $1·5$—2 D of myopia would demand an aqueous index equal to or greater than that of the cornea. The increase in the aqueous index in iritis has been determined by Bajardi as $0·003$—$0·005$, which is quite insufficient measurably to affect the total refraction of the eye. Repeated paracenteses have produced an increase in the index of the aqueous of $0·0085$. Moauro found the refractive index of the aqueous increased by $0·018$ in dogs whose bile-ducts had been tied, which would be equivalent to a myopia of only $0·75$ D even if the vitreous were not similarly affected. Increase in the vitreous index would counteract the effect. The myopia of diabetes cannot be explained by increase in the aqueous index. The aqueous would have to contain 20 per cent. of sugar in order that its refractive index might be raised to that of the cornea (Lohnstein), a result which would only cause a myopia of $1·5$ D in a previously emmetropic eye. Moreover, a concentration of sugar of 5 per cent. would cause opacity in the lens (Deutschmann) (v. Vol. II, p. 426).

Lenticular index myopia may be due to too high an index of the nucleus, too low an index of the cortex, or to both causes. The total refractive index of the lens tends to rise in old age, possibly more particularly as a promontory sign of senile cataract. This was first pointed out by Henry in 1786. The amount of myopia may be considerable. Rydel records the case of a man who, having had to use convex glasses for presbyopia, developed $4·5$ D of myopia at 72 years of age. Landesberg observed myopia of $1·5$—10 D in seven patients, and Fuchs of 1—9 D in eleven patients. Herrnheiser observed a myopia of 7 D at 80 years of age in a previously emmetropic woman. Similar cases have been described by Weber, Critchett, Snellen, de Wecker, Burnett, and others. Mauthner saw a case in which the myopia developed in a few hours as

the result of exposure to a very bright light. This rise in refraction is to be attributed to increased total refractive index of the lens, due especially to increased index of the nucleus. Heine found the total index of the lens in an old myope to be 1·451 in one eye, 1·47 in the other, there being no axial elongation of the eyes.

The myopia of diabetes is due to changes in the lens (Hirschberg), and is independent of cataractous changes. The sudden onset of myopia in patients about fifty years of age without opacity is very suspicious (Hirschberg). The myopia may reach several dioptres. Cases have been recorded by Grimsdale, Doyne, Roosa, Risley, and others. In Risley's case stronger (1—3 D) glasses were necessary when there was no sugar in the urine than when it was absent.

Rarely a diminution in refraction has been observed at the periods when sugar has been present in the urine (Landolt, Sourdille). Landolt attributes this to increased refractive index of the vitreous, Sourdille to softening and shrinking of the eye.

There is no evidence to determine whether any of the myopia of diabetes is due to increased curvature of the lens surfaces, though it is not improbable if absorption of water takes place.

Vitreous index myopia, due to diminution in the refractive index of the vitreous, has not yet been demonstrated.

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CHAPTER XVI

HYPERMETROPIA AND ASTIGMATISM

HYPERMETROPIA

HYPERMETROPIA is that dioptric condition of the eye in which, with the accommodation at rest, incident parallel rays come to a focus posterior to the light-sensitive layer of the retina.

Hypermetropia may be due, theoretically, to any of the following conditions:

A. Abnormal shortness of the eye—*axial hypermetropia*.

B. Abnormal curvature of the refracting surfaces—*curvature hypermetropia*:

    (*a*) Too slight curvature of the cornea.

    (*b*) Too slight curvature of one or both surfaces of the lens.

C. Abnormal refractive index of the media—*index hypermetropia*.

    (*a*) Too low index of the cornea or aqueous.

    (*b*) Too low total index of the lens, due to

        (*a*) Too low index of the nucleus.

        (β) Too high index of the cortex.

        (γ) Both these causes.

    (*c*) Too high index of the vitreous.

D. Abnormal position of the lens—*i. e.* displacement backwards.

E. Absence of the lens.

F. A combination of the above abnormalities.

The possibility of the condition of refraction which is now called hypermetropia was first asserted by the mathematician Kästner (1755); from the resemblance to presbyopia he termed the condition "hyper-presbytas," a name which was used as late as 1855 by Stellwag. Janin (1772) compared the condition with that found after operation for cataract, and Olbers (1780) and Listing (1845) discussed the optical problem. Ware (1813), Weller (1821), Ritterich (1843), Sichel (1845), Fronmüller (1850), and Cooper (1853), among early writers, investigated the clinical condition. The modern period may be said to commence with Stellwag v. Carion (1855), who contributed an important paper on the errors of accommodation of the eye, but the subject was first put upon a sound basis by Donders (1858), who introduced the term "hyper-metropia," and distinguished between this condition and presbyopia.

Helmholtz had previously used the term " hyperopia," which still finds favour with American writers.

Axial hypermetropia is the commonest form found clinically. It comparatively rarely exceeds 6—7 D, which is equivalent to a shortening of the optic axis of 2 mm. Individual cases of high hypermetropia without other anomaly, such as coloboma or microphthalmia, have been recorded—*e.g.* 14 D (Marple), 15 D (Work Dodd), 20 D (Schön), 24 D (Seabrock).

The fundus may exhibit no abnormality. A bright reflex, suggesting the appearance of watered silk, is commoner in hypermetropic than in emmetropic or myopic eyes, but is not confined to them. Tortuosity of the retinal vessels is also more frequently observed in hypermetropic eyes than in others (Benson, Nettleship, Stephen Mackenzie), and may be regarded as due to the diminished area which the retina has to cover; it is however generally absent, and is not infrequently observed in eyes which are not hypermetropic. There is no reason to suppose that the physiological cup in the optic disc is commoner in hypermetropia than in other refractive conditions. The investigations of Herrnheiser and Hess have disproved the relationship which was enunciated by Schön, and was attributed by him to the dragging effect of accommodation. More important is the pseudoneuritis which has been often observed. Stephen Mackenzie (1884) first described slight redness and swelling of the disc, with blurring of the edges. The observation was confirmed by Bristowe, Marcus Gunn, Arnfeld, Nottbeck, Holmes Spicer, and others. The condition is not a neuritis, as was at first thought (neuritis hypermetropum), but remains unchanged for an indefinite time, and is not associated with visual defects. Bristowe found the condition in 23·2 per cent. of hypermetropes, but about 3 per cent. (Nottbeck) is probably more accurate. It is much commoner in hypermetropia than in emmetropia or myopia; thus Nottbeck found hypermetropia of 1—7 D in 34 cases out of 37. No relationship between the ophthalmoscopic appearances and the degree of hypermetropia can be made out, nor is the condition affected by correction with glasses; hence it probably has nothing to do with over-accommodation. The pseudoneuritis is probably congenital (Nottbeck). Adamück described a retinitis idiopathica as frequent in hypermetropia, and Dobrowolski reported a case with retinal hæmorrhages which rapidly cleared up on correcting the refraction. These observations have not been confirmed.

Anatomical investigation shows that the hypermetropic eye is not only shorter but usually smaller than the emmetropic. The changes are not confined to the posterior segment, as in most myopic eyes. The cornea may be normal, but its diameter is often reduced ; it frequently shows anomalies of curvature, especially regular astigmatism. The anterior chamber is shallower than normal; this is due partly to the relatively larger size of the lens (*see* " Glaucoma "), and partly to increased curvature of the lens brought about by increase in the tonic contraction of the ciliary muscle. Iwanoff described the ciliary muscle in hypermetropic eyes as consisting of hypertrophied circular fibres (Müller's muscle) and relatively atrophied meridional fibres (Brücke's muscle).

It has already been pointed out that the condition of the ciliary muscle shows great variations even at birth, and independently of the refraction (v. p. 913). It must not be forgotten that in hypermetropic eyes the muscle may be fixed in a more or less contracted condition (Hess).

No anatomical abnormalities have been described in the retina, choroid, or optic nerve in hypermetropia. It is possible that there are slight defects in the development of the percipient elements of the retina, since the visual acuity is often diminished. This was explained by Donders on the grounds that perfect visual acuity would demand the presence in a smaller area of retina of a number of percipient elements equal to those possessed by the emmetropic eye. Mauthner has shown that the difference is inappreciable.

In pathological conditions the retina may be displaced forwards, producing hypermetropia. This sometimes occurs as the result of the pressure of orbital growths (q.v.) (Hirschberg, Leber, Haab, etc). It has been suggested that hypermetropia may follow diminution of the contents of the globe (e.g. in diabetes, Horner), and Snellen observed high hypermetropia after rupture of the cornea and sclerotic, with prolapse of vitreous. More common is the hypermetropia of detached retina, though the retina seldom retains its functions for any considerable period under these conditions. Horner records a case of detachment in an eye with 8 D of myopia; the refraction diminished in the course of four weeks to a hypermetropia of 1 D.

The new-born are almost invariably hypermetropic. Herrnheiser found variations from 1 to 6 D, with a mean of 2·3 D, thus confirming Horstmann's earlier estimate. Straub and Falkenburg give a mean of 3 D. In the first decades of life the hypermetropia curve falls rapidly, remaining at about 50 per cent. after the twentieth year (Fig. 665). Randall found 92 per cent. hypermetropes amongst 1754 children in the first years of life, and 76 per cent. amongst 3358 in the first years of schooling; in higher schools at least 56 per cent. were hypermetropic.

The refraction apparently changes little with increased growth, though some change is appreciable (Hasner, Randall, Herrnheiser, Straub). Hasner considers that the hypermetropia diminishes about 1 D in five years.

Hypermetropia shows no predilection for either sex. As regards racial variations it is a well-known fact that savages are usually hypermetropic, though accurate statistics are wanting. The higher mammals, especially the carnivora, are also hypermetropic.

Curvature and index hypermetropia are rare. It has already been shown that there is no definite relationship between the radius of the corneal curvature and the refraction of the eye (v. p. 928). Acquired corneal curvature hypermetropia is occasionally found as the result of the contraction of the scars of wounds or ulcers. Such cases have been reported by Mauthner, Axenfeld, Weiss, Hirschberg, and others. In a case of Axenfeld's there was a central hypermetropia of 5 D and a peripheral myopia of 7 D; correction of either gave a visual acuity of $\frac{6}{18}$—$\frac{6}{12}$. The cornea is rarely sufficiently clear under these circumstances to allow of any improvement with correction.

The hypermetropia which comes on in old age associated with presbyopia is to be attributed to increased refractive index of the cortex of the lens. Straub and Falkenburg consider that it is a dynamic hypermetropia, due to loss of tone in the ciliary muscle.

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ASTIGMATISM

Astigmatism is that condition of refraction in which a point of light does not produce a punctate image upon the retina. Strictly according to this definition no eye is stigmatic, since chromatic and spherical aberration prevent the formation of an absolutely punctate image. The more pronounced forms of astigmatism were first investigated by Thomas Young (1793), who proved that his own eye was astigmatic. Since the astigmatism was not abolished by eliminating the corneal refraction by placing the eye in water, it was attributed to the lens, and indeed to an oblique position of the lens. This alone would scarcely suffice to account for the amount of distortion, which was probably due to differences of curvature of the surfaces of the lens in the chief meridians (Gullstrand). Fischer (1810) and Airy (1827) also investigated the astigmatism of their own eyes, and Gerson (1810) first proved the occurrence of corneal astigmatism. The optical conditions were expounded by Hamilton (1828), Sturm (1838), Schultén (1845), Kummer, Matthiessen, Böklen, Leroy, and others. Donders and Knapp (1862) showed the frequent occurrence of astigmatism in human eyes, and the former divided the condition into two forms, regular and irregular. In *regular astigmatism* the deviation of the refracting surfaces from the spherical form is such that mathematical investigation of the refracted rays and correction by cylindrical glasses are possible. Usually the cornea is most at fault, the curvature being toric, such that whilst the vertical and horizontal meridians are circular the radius of curvature of the former is less than that of the latter. When the radius of curvature of the vertical meridian is greater than

that of the horizontal the astigmatism is said to be against the rule. Other anomalies of regular astigmatism consist in obliquity of the principal meridians or axes. In these forms of regular astigmatism the refracted rays of a perpendicularly incident bundle form a conoid (Sturm) with two planes of symmetry; hence the condition has been called astigmatism without asymmetry (Gullstrand). Another form was described by Javal as due to "cornée décentrée," and has been investigated by Sulzer and Gullstrand; here there is astigmatism with asymmetry or decentration. It is beyond the scope of this work to describe the various optical conditions which have been observed; they have been exhaustively expounded by many writers, but especially of late years by Gullstrand. Whilst the cornea is responsible for the greater part of the astigmatism, in most cases the effect of the lens cannot be left out of account, since it markedly affects the total astigmatism (Young, Tscherning, Awerbach, Javal, Schiötz, Chibret, Dimmer, Pfalz, and others).

Steiger found that in two thirds of all eyes there was an astigmatism of 0·5—1·0 D, or in seven eighths of 0·25—1·25 D. In 95·7 per cent. of children the axes were according to the rule. The frequency of astigmatism against the rule increases gradually to the seventieth year, and afterwards more rapidly. Schön found the percentage of eyes with inverse astigmatism increase from 11·6 per cent. in youth to 68·3 per cent. in old age. Hess found scarcely 1 per cent. of cases of astigmatism from 6 to 14 years of age against the rule; in the same period there was no decrease in direct astigmatism: in 10—12 per cent. of all children the total astigmatism amounted to at least 1 D. Nordenson found in school children 77 per cent. direct, 1·3 per cent. indirect, astigmatism; 12 per cent. with oblique axes, 4·4 per cent. without corneal astigmatism; 30 per cent. had astigmatism of at least 1 D, 1·7 per cent. more than 1·5 D. Pflüger found astigmatism against the rule more common in females—11 : 9; according to Steiger astigmatism is generally somewhat greater in women than in men. In most cases the axes are symmetrical in the two eyes—1307 : 458 cases (Risley and Thorington): The difference in refraction between the two meridians seldom exceeds 5—6 D: rare cases in which cylinders of 10 D and even 20 D have been worn are reported (Schneidemann, Despagnet).

The ordinary forms of astigmatism must be regarded as a congenital anomaly. The influence of the intra-ocular pressure upon the corneal curvature has been often investigated (Schelske, Laqueur, Eissen, Bajardi, Lucciola). Helmholtz found that the corneal curvature was greater in excised eyes than in the living eye, and that the cornea became flatter on injecting water into the vitreous chamber. These observations were confirmed on animals' eyes by Schelske and Laqueur, who found that all diameters were increased. The results were not, however, constant, for Schelske found that the corneal radius, after increasing for a time, became diminished on further increasing the pressure; it then remained constant awhile, again increasing with the greater pressures. Eissen showed that in rabbits a rise of tension of 5—10 mm. often, and of 25 mm. constantly, caused changes. Usually all meridians were altered; with gradual increase of pressure astigma-

tism at first increased, then diminished, so that a normal astigmatism might give place to an inverse. Astigmatism against the rule has frequently been observed in human glaucomatous eyes, in 41—50 per cent. as compared with 2·2 per cent. in normal eyes (Schön, Pfalz, Martin). The cause of the change in astigmatism with increasing age is unknown. Eissen attributed it to change in tension, Schön to the influence of partial contraction of the ciliary muscle upon the shape of the cornea. v. Reuss in 1877 conjectured that contraction of the ciliary muscle could alter the curvature of the cornea ; he found that under strong eserin there was a diminution in the radius of the cornea of 0·04—0·14 mm. Carhart considered that strong efforts of accommodation in a sound eye or ordinary accommodation in a weak eye might produce stretching of the walls, leading to lengthening of the axis and changes in the curvature of the cornea. Steiger pointed out that the constancy of the astigmatism in the plastic eyes of young children was against this view. Gullstrand found in myopia extreme variations in the corneal curvature which might be attributed to stretching of the globe.

Partial contraction of the ciliary muscle has been invoked to account for the difference between the corneal and the total astigmatism. Change in astigmatism with variations in the pupillary diameter have been held to support the theory. The view has been upheld by Giraud-Teulon, Dobrowolski, Woinow, Martin, Pflüger and Mauthner, and others, whilst it has been opposed by Bull, Sulzer, Tscherning, Eriksen, Hess, and others. Hess points out many faults in the methods of observation—e. g. the size of the object, movement of the eye, the effect of the lids as a stenopœic slit, etc. That lid-pressure can cause change in the corneal curvature was shown by Botwinnik, and confirmed by Bull, Gullstrand, and Howe. It is not improbable that this is a factor in the pathogenesis of astigmatism. Even stretching the lids with the finger can effect a considerable change in the cornea, as shown ophthalmometrically by Laqueur (1884) and Weiss (1886).

Schön, Javal, Roure, Vacher, and others have conjectured an ætiological relationship between astigmatism, and especially partial ciliary contraction, and cataract formation. Thus in unequal astigmatism the more affected eye has been said to become cataractous sooner and the cataract is said to progress more rapidly. Schön's statement that equatorial cataract begins in the horizontal meridian is denied by Hess.

A form of regular astigmatism following wounds, especially extraction and iridectomy wounds, was first described by Donders (1864). With superior or inferior sections it is usually against the rule, as was pointed out by Haase. The larger the wound and the nearer the middle of the cornea, the greater is usually the astigmatism. It is more marked and less regular when normal healing is interfered with, as by prolapse of iris, etc. Exact ophthalmometric observations on wound astigmatism were first made by v. Reuss and Woinow (1869), later by Mauthner, Dolganoff, Pfingst, Scimeni, Treutler, and others. Treutler in 49 cases seven days after extraction found the vertical meridian diminished in 88 per cent., unchanged in 2 per cent., increased in 10 per cent.; the horizontal meridian was increased in 88 per cent., un-

changed in 2 per cent., diminished in 10 per cent. The highest diminution in the radius of the vertical meridian was 1·5 mm., the highest increase in the horizontal more than 1·8 mm. The following mean changes are given:

	Vertical meridian.		Horizontal meridian.
v. Reuss	0·3 mm.	.	− 0·27 mm.
Weiss	0·45 ,,	.	− 0·02 ,,
Dolganoff	0·44 ,,	.	− 0·47 ,,
Treutler	0·7 ,,	.	− 1·1 ,,

The smaller results obtained by v. Reuss, Weiss, and Dolganoff are probably due to the length of time after operation—13 to 16 days. The astigmatism is greatest soon after operation, diminishes rapidly at first, then very slowly. Treutler found a change still going on after four months. As the final result Dolganoff found the horizontal meridian in 18 cases increased 2·2 D, in 2 cases diminished 0·25—0·5 D; the vertical meridian was unchanged in 3 cases, increased 0·25—1·25 D in 4, diminished on an average 1·7 D in 13. As Hess points out, these observations upon wound astigmatism confirm his investigations of striate opacity (v. Vol. I, p. 180).

Regular astigmatism may occasionally follow wounds other than those made by operation, and also ulcers. Hirschberg, Dufour, and Evers have described it after episcleritis or sclerosing keratitis.

In *irregular astigmatism* the refracted rays have no planes of symmetry. The condition is usually due to the irregular shrinking of scars such as are caused by ulcers or lacerated wounds. It may also be due to keratoconus, lenticonus, etc.

*THOMAS YOUNG.— Phil. Trans., lxxxiii, 1793; Œuvres ophth. de T. Young par Tscherning, Copenhague, 1894. GERSON.—See K. M. f. A., iv, 1866. AIRY.—Cambridge Phil. Soc. Trans., 1827. HAMILTON.—Roy. Irish Acad. Trans., xv, 1828; xvi, 1831; xvii, 1837. STURM.—Jl. de Math., 1838; Comptes rendus, xx, 1845. SCHULTÉN.—Mém. de l'Acad. impériale de St. Petersbourg, iv, 1845. WHARTON JONES.—Proc. Roy. Soc., x, 1860. DONDERS.—A. f. O., vii, 1861; Astigmatismus, Berlin, 1862; Anomalien der Refraction u. Accommodation, Wien, 1866. JAVAL.—Ann d'Oc., liii, 1863; Soc. de Biol., 1873, 1879; Ann. d'Oc., lxxxvii, lxxxviii, 1882; xcvii, 1887; Mém. d'Ophtalmométrie, Paris, 1891. KNAPP.—A. f. O., viii, 2, 1866; Ophth. Rev., 1887; T. Am. O. S., 1892; Z. f. A., ii, 1899. DOBROWOLSKI.—A. f. O., xiv, 3, 1868. v. REUSS AND WOINOW.—Ophthalmometrische Studien, Wien, 1869. WOINOW.—A. f. O., xv, 2, 1870; K. M. f. A., ix, 1871. HULKE.— R. L. O. H. Rep., viii, 1875. SCHÖN.—B. d. o. G., 1877; Die Funktionskrankheiten des Auges, Wiesbaden, 1893. WEISS.—A. f. A., vi, 1877; Ann. d'Oc., cxv, 1896. LEROY.— Comptes rendus, xc, 1880; A. d'O., i, 1881; Rev. gén. d'O., 1882; Arch. de Physiol., xxi, 1889. SCHIÖTZ.—Congrès d'O., Milan, 1881; A. f. A., xv, 1885. MATHIESSEN.—Centralz. f. Opt. u. Mech., 1882; K. M. f. A., xxi, 1883; A. f. O., xxix, 1, 1883; Pflüger's Archiv, xxxii, 1883. MARTIN.—Ann. d'Oc., xc, 1883; xci, 1884; A. d'O., v, 1885; Ann. d'Oc., xciii, 1885; xcv, 1886; xcvii, 1887; ciii, 1890; cxiii, 1895. NORDENSON.—Ann. d'Oc., lxxxix, 1883. PFALZ.—C. f. A., ix, 1885; A. f. O., xxxi, 1, 1885; Internat. Congress, Utrecht, 1899; Ophth. Klin., 1899. PRIESTLEY SMITH.—Ophth. Rev., iv, 1885. THEOBALD.—T. Amer. O. S., 1885. CHIBRET.—Ann. d'Oc., xcv, 1886; A. d'O., x, 1890; xiv, 1894; Soc. franç. d'O., 1894. v. HELMHOLTZ.—A. f. O., i, 2, 1855. SCHELSKE.—A. f. O., x, 2, 1864. LAQUEUR. —A. f. O., xxx, 1, 1884. EISSEN.—A. f. O., xxxiv, 2, 1888. EMERSON.—T. Amer. O. S., 1888. EXNER.—A. f. O., xxxiv, 1, 1888. IMBERT.—Gaz. hebd., 1888. AHRENS.—K. M. f. A., xxvii, 1889. BULL.—Rev. gén. d'O., 1889; B. d. o. G., 1892; A. d'O., xvi, 1896. SCIMENI. Ann. di Ott., xviii, 1889. *GULLSTRAND.—Skand. Archiv f. Physiol., ii, 1890; A. f. O., liii, 2, 1901. PFLÜGER.—Internat. med. Congr., Berlin, 1890. BAJARDI.—Atenea med. Parmense, iv, 1891; Ann. di Ott., xxii, 1893. SULZER.—Soc. franç. d'O., 1891. HARLAN.—T. Am. O. S., 1892; A. of O., xxii, 1893. AXENFELD.—K. M. f. A., xxxi, 1893. G. J. BULL.— Internat. Congress, Edinburgh, 1894. DOLGANOFF.—A. f. A., xxix, 1894. HESS AND

Diederichs.—A. f. A., xxix, 1894. Howe.—Amer. Jl. of O., 1894. Steiger.—A. f. A., xxix, 1894; xxxvi, 1897; Korrespondenzbl. f. Schweizer Aerzte, 1897. Antonelli.—Ann. di Ott., xxiv, 1895. Jackson.—Med. News, 1895. Roure.—A. d'O., xv, 1895. *Hess.— A. f. O., xlii, 2, 1896; xliii, 1, 1897; in G.-S., viii, 2, 1903 (Bibliography). Pfingst.— A. of O., xxv, 1896. Risley and Thorington.—Jl. of Amer. Med. Assoc., 1896. Asch-heim.—K. M. f. A., xxxv, 1897. D'Aubigné-Carhart.—New York Med. Jl., 1897. Despagnet.—Ann. d'Oc., cxviii, 1897. Ellis.—A. f. A., xxxiv, 1897. Gradle.—A. f. O., xliii, 1, 1897. Evers.—K. M. f. A., xxxvi, 1898. Lans.—A. f. O., xlv, 1, 1898. Swan Burnett.—Amer. Jl. of O., 1899. Clark.—Ophth. Rev., 1899. Reymond.—Internat. Congr., Utrecht, 1899; Z. f. A., ii, 1899. Schneidemann.—Ophth. Rev., 1899. Awer-bach.—Ges. d. Augenärzte, Moskau, 1900.

CHAPTER XVII

THE CIRCULATION OF THE EYE

ANATOMY

Arteries.—The ocular blood supply in man is derived almost entirely from the internal carotid artery, whilst it is within the skull. This is not the case in lower mammals; and as all experimental investigation must be made upon these, it is essential to determine accurately the differences which obtain.

The general tendency as we ascend the animal scale is for the principal ophthalmic artery, which in the lower members is derived from the external carotid, to be derived from the internal carotid. On the border line there are usually two or more ophthalmic arteries—generally one derived from each source, and there is commonly an anastomotic branch linking the two systems. It is only to be expected that individual variations should be of frequent occurrence, and such is the case.

Rabbit.—The common carotid in the rabbit gives off the thyroid artery and the ascending pharyngeal (Fig. 666). At the level of the hypoglossal nerve the artery divides into the internal and external carotids. The former is much the smaller, runs without branching to the bulla tympani, and enters the skull by the carotid foramen. It then winds round the lateral side of the body of the sphenoid bone, and after crossing the oculo-motor nerve, gives off the anterior communicating and superior ophthalmic arteries. It ends by dividing into the anterior and middle cerebral. In four out of six dissections one was able to trace a fine branch of communication between the internal carotid, as it lies on the side of the body of the sphenoid, and the internal maxillary close to the origin of the inferior ophthalmic artery. The external carotid gives from its inner side the laryngeal, lingual, and external maxillary in that order from below upwards. The last-named artery gives off the facial. From the posterior wall is given off the occipital. A little below the neck of the jaw the artery divides into the superficial temporal and the internal maxillary. The former gives off the transverse facial and the auricular. The internal maxillary runs deep to the internal pterygoid behind the lower jaw. It gives off the tympanic, the inferior alveolar, some muscular branches, and the middle meningeal. It then passes through the pterygoid canal, and gives off the

inferior ophthalmic. It ends by supplying a superior alveolar branch and divides into the infra-orbital and pterygo-palatine arteries.

So far in these dissections the arrangement of the branches of the carotid arteries is in entire agreement with the description given by Krause. I have therefore followed his nomenclature. I now quote in full his description of the ophthalmic arteries (Fig. 667).

" The inferior ophthalmic artery runs on the anterior surface of the upper part of the great wing of the sphenoid, bends forward over the optic nerve, and reaches its anterior side. It then anastomoses with the superior ophthalmic artery. Its branches are as follows: (1) Lacrymal, which appears through the posterior supra-orbital foramen as the supra-orbital artery. (2) Frontal, which in the same way goes through the anterior supra-orbital foramen. Immediately after its origin it usually gives off the well-developed anterior ethmoidal artery which goes through
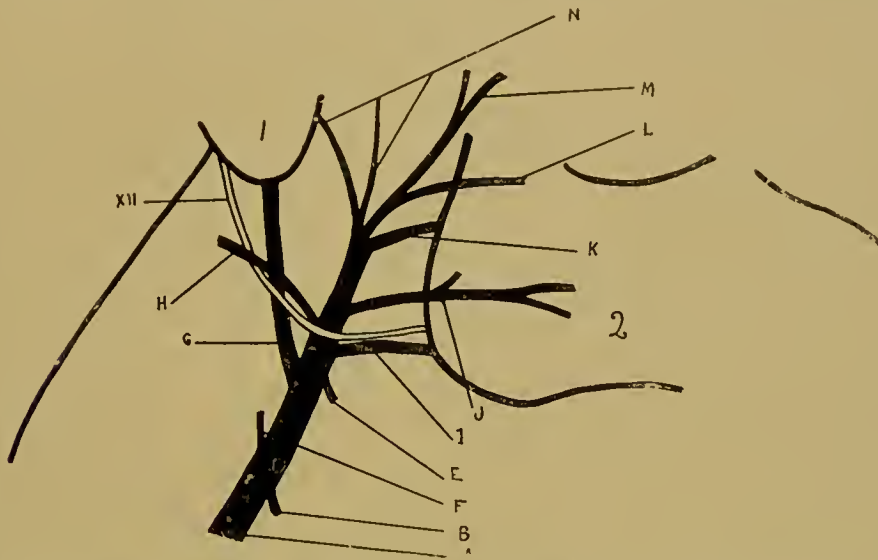
Fig. 666.—Scheme of the Carotid Arteries in the Rabbit.

Henderson, R. L. O. H. Rep., xv. A. Common carotid artery. B. Thyroid artery. E. Laryngeal artery. F. Ascending pharyngeal artery. G. Internal carotid artery. H. Occipital artery. I. Lingual artery. J. External maxillary artery. K. Internal maxillary artery. L. Transverse facial artery. M. Superficial temporal artery. N. Auricular artery. XII. Hypoglossal nerve. 1. Placed on the bulla tympani. 2. On the lower jaw.

the ethmoidal foramen into the nasal cavity. (3) Muscular branches to the eye muscles.

The superior ophthalmic artery is but little developed. It runs forward to the optic foramen, and goes through this on the under and lateral side of the optic nerve into the orbit, winds under the nerve to its anterior side, and anastomoses with the inferior ophthalmic artery. It gives off the ciliary arteries and the central artery of the retina." (Krause.)

In two of the dissections there was no anastomosis between the two ophthalmic arteries in the situation here described. In both these cases the anastomotic branch between the internal carotid and the inferior ophthalmic was present. In two others this anastomotic branch was also present, and in these the superior ophthalmic artery was very small.

Dog.—In the dog the carotid artery gives off as its first branch a thyroid artery (Fig. 668). A muscular branch to the sternomastoid usually arises at about the same level as the thyroid. A little higher the ascending pharyngeal and the laryngeal arise. The artery now divides into the internal and external carotids. The internal carotid is always the first postero-external branch (Fig. 669). It takes origin just at the level of the hypoglossal nerve. It is most easily reached in the living animal by retracting the common carotid outwards, and tracing up its inner side. There is always present an enlargement close to its origin.

The artery runs straight up with the vagus to the bulla, and enters the skull through the carotid foramen. It gives no branches in the neck. The external carotid gives as its first branch on the outer side
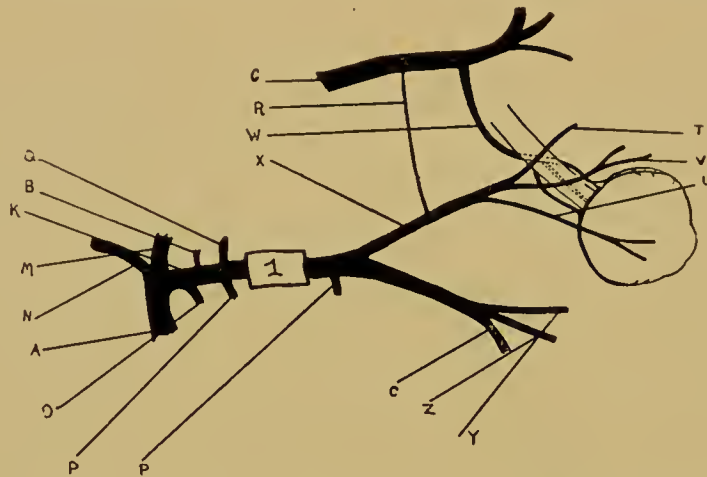
FIG. 667.—SCHEME OF THE INTERNAL MAXILLARY AND OPHTHALMIC ARTERIES OF THE RABBIT.

Henderson, R. L. O. H. Rep., xv. A. External carotid artery. B. Tympanic artery. C. Superior alveolar artery. G. Internal carotid artery. K. Internal maxillary artery. M. Superficial temporal artery. N. Auricular artery. O. Inferior alveolar artery. P. Muscular arteries. Q. Middle meningeal artery. R. Ramus anastomoticus. T. Ethmoidal artery. U. Lacrymal artery. V. Frontal artery. W. Superior ophthalmic artery. X. Inferior ophthalmic artery. Y. Infra-orbital artery. Z. Pterygopalatine artery. I. Placed on the pterygoid canal.

the occipital. This artery arises close to the internal carotid, and is of about the same size. In the living animal it may be readily mistaken for it. It is somewhat more superficial in origin, and will usually be found to give an anterior branch soon after its origin. The next branch, and one of the largest, is the lingual. Then comes the external maxillary, from which is derived the facial. The artery then breaks up into the superficial temporal, auricular, and internal maxillary arteries. The internal maxillary winds round the maxillary joint over the bulla, enters the pterygoid canal, and ends after leaving this by dividing into the infra-orbital and palatine branches. Its branches may be divided into two sets : those given off before it enters the pterygoid canal, and those given off after it leaves it. The first set comprise the middle meningeal, the deep temporals, the inferior alveolar, and the muscular. The

second set comprise a further set of muscular branches and the inferior ophthalmic (Fig. 670).

" The ophthalmic artery springs from the internal maxillary after it
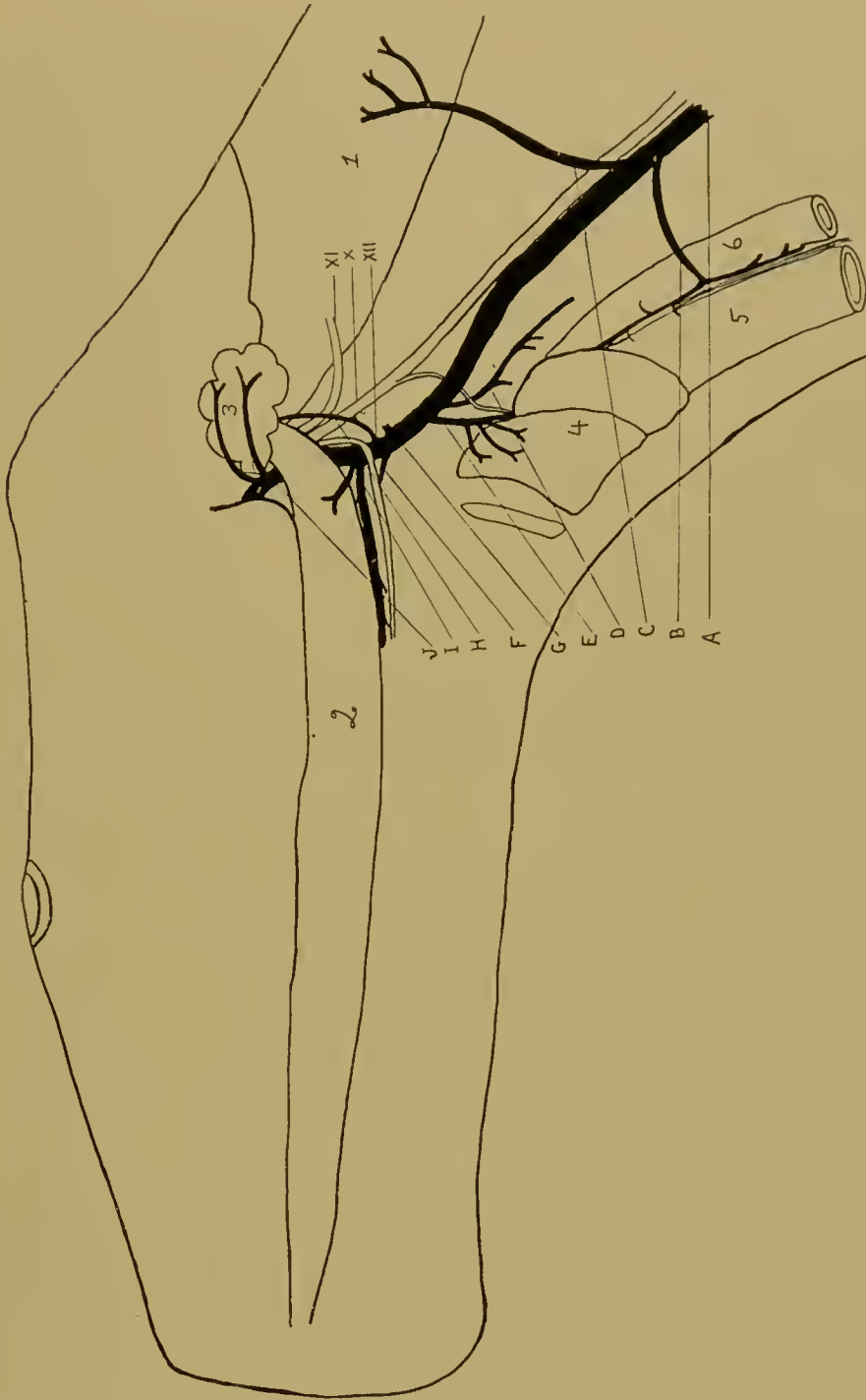
Fig. 668.—Scheme of the Carotid Arteries in the Dog.

Henderson, R. L. O. H. Rep., xv. A. Common carotid artery. B. Thyroid artery. C. Muscular branch to sterno-mastoid. D. Muscular branch to deep neck muscles. E. Laryngeal artery. F. Ascending pharyngeal artery. G. Internal carotid artery. H. Occipital artery. I. Lingual artery. J. External maxillary artery. X, XI, XII. Vagus, spinal accessory, and hypoglossal nerves. 1. Placed on the sterno-mastoid. 2. On the digastric. 3. On the salivary gland. 4. On the larynx. 5. On the trachea. 6. On the œsophagus.

has left the pterygoid canal, and next runs between the peri-orbita and the temporal muscle, and further in on the orbital part of the frontal bone on the outer side of the peri-orbita to the ethmoidal foramen. Through this it runs into the skull as the ethmoidal artery. Shortly

after its origin it, or one of its muscular branches, gives an anastomotic branch, which goes to the internal carotid. This, according to Bellarminow, who calls it the internal ophthalmic artery, gives off the central artery of the retina." (Ellenberger and Baum.)

In none of our dissections has this arrangement been exactly followed (Figs. 671, 672, and 673). In all of them the anastomotic branch from the internal carotid has entered the internal maxillary immediately before the origin of the inferior ophthalmic artery, and this latter has in all been represented by two separate branches. In consideration of the conditions found in the rabbit it is wiser to adhere to the terms "superior" and "inferior," although Bellarminow's division into internal
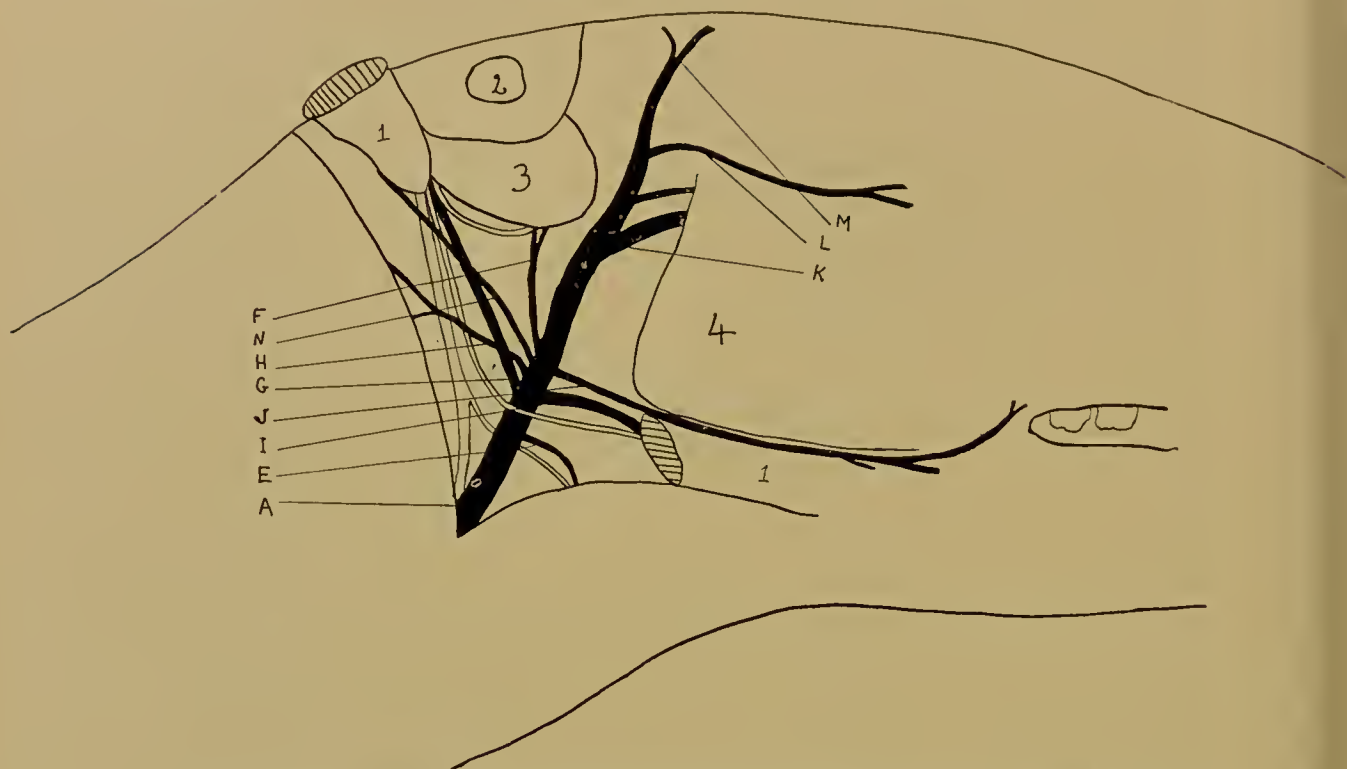
Fig. 669.—Scheme of Carotid Arteries in the Dog, traced higher after Division of the Digastric.

Henderson, R. L. O. H. Rep., xv. A to N. As in Fig. 668. 1. Placed on the digastric. 2. On the ear. 3. On the bulla tympani. 4. On the lower jaw.

and external has the advantage of indicating their source from the internal and external carotids respectively. In only half the dissections has there been present a superior ophthalmic artery arising from the ramus anastomoticus. In the remaining half this artery has been derived from the internal carotid after the main trunk has left the internal carotid, and has entered the orbit through the optic foramen. The anastomotic branch is always of very fair size, and arising immediately after the internal carotid has reached the cavernous sinus, passes through the fissura orbitalis below the first division of the fifth nerve. In two dogs a large meningeal branch has arisen from the ramus anastomoticus on both sides. This branch has apparently taken in these cases the place of the middle meningeal.

If the anastomotic branch always supplied the interior of the eye it is certainly of sufficient size to maintain the circulation, and as blood reaches it equally from the internal maxillary and internal carotid, it is probable that the supply to the eye would not suffer from the loss of only one of these sources. This, however, as has been shown, is not invariably the case. But in those cases in which the ciliary arteries and the central artery of the retina have been derived from a superior ophthalmic artery arising from the internal carotid a free anastomosis has always been present between this superior ophthalmic artery and
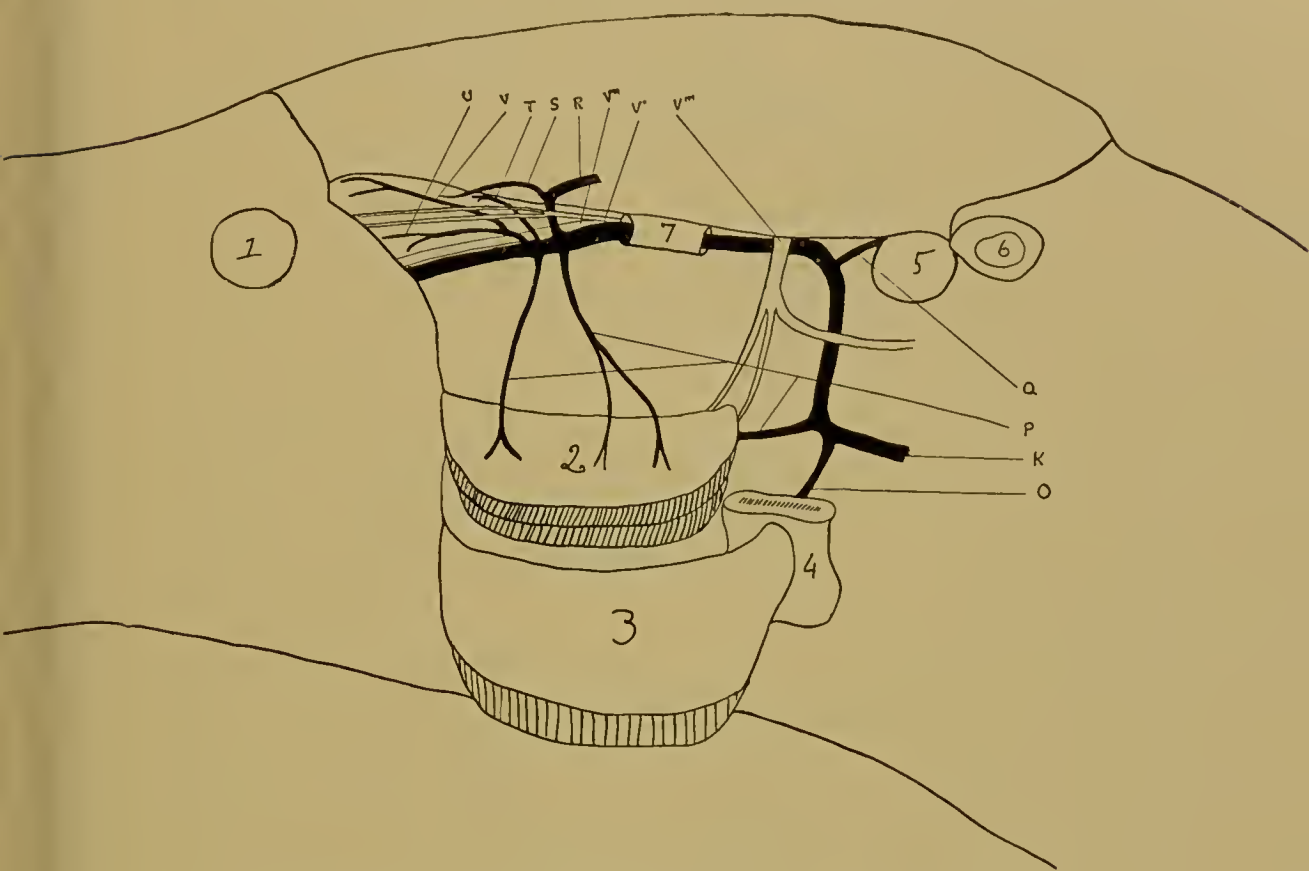
FIG. 670.—SCHEME OF INTERNAL MAXILLARY AND OPHTHALMIC ARTERIES IN THE DOG.

Henderson, R. L. O. H. Rep., xv. K. Internal maxillary artery. O. Inferior alveolar artery. P. Deep temporal artery. Q. Middle meningeal artery. R. Ramus anastomoticus. S, Superior ophthalmic artery (inferior of Bellarminow). T. Ethmoidal artery. U. Lacrymal artery. V. Frontal artery. v′, v″, v‴. The three parts of the fifth nerve. 1. Placed on the eye. 2. On the temporal and pterygoid muscles, cut and turned down. 3. On the masseter, also turned down. 4. On the lower jaw. 5. On the bulla tympani. 6. On the ear. 7. On the pterygoid canal.

one of the branches of the inferior ophthalmic artery. It is, then, even in these cases, anatomically possible for the intra-ocular circulation to be maintained in the absence of one or other of the ophthalmic arteries.

Man.—In man the arteries to the eye are derived almost exclusively from the internal carotid artery as it lies within the skull. It is unnecessary in this place to enter into details as to the origin and

distribution of the various branches in their course outside the eye (*see* Quain's 'Anatomy,' Figs. 344, 345).

Fig. 671.
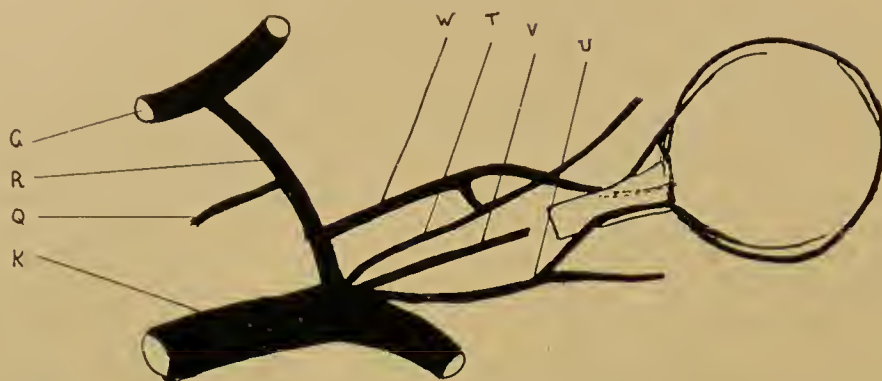
Fig. 672.

Fig. 673.

Figs. 671, 672, and 673.—Variations in the Orbital Arteries in the Dog. Henderson, R. L. O. H. Rep., xv. G. Internal carotid. K. Internal maxillary artery. Q. Middle meningeal artery. R. Ramus anastomoticus. W. Superior ophthalmic artery. X. Inferior ophthalmic artery. T. Ethmoidal artery. U. Lacrymal artery. V. Frontal artery.

The anastomoses between branches of the ophthalmic artery and those of the external carotid are very few and very small. On the authority of Quain's 'Anatomy':

(1) The central artery of the retina usually arises in common with the internal ciliary trunk, sometimes with the external. No anastomoses. (2) Ciliary arteries: (*a*) posterior from ophthalmic; (*b*) anterior from muscular and lacrymal. The former have no anastomoses and the latter no direct one. (3) Lacrymal. This anastomoses with the anterior deep temporal and transverse facial, and through the outer end of the sphenoidal fissure with the middle meningeal. (4) Recurrent branch to anastomose with internal carotid. (5) Muscular branches. Some anastomoses between the infra-orbital and these branches must take place in the substance of the inferior oblique, but are not directly mentioned. (6) Supra-orbital. This anastomoses with superficial temporal. (7) Anterior and posterior ethmoidal. No anastomoses given. (8) Palpebrals. No anastomoses given. (9) Nasals. Anastomose with facial. (10) Frontals. No anastomoses given.

The following variations are also enumerated. The ophthalmic artery may enter the orbit through the sphenoidal fissure. The lacrymal artery not infrequently, and in rare cases a large part, or even the whole, of the ophthalmic artery itself arises from the middle meningeal. The lacrymal artery may also be reinforced by the anterior deep temporal artery. The ophthalmic artery has been seen to give off the middle meningeal.

Fr. Meyer, in discussing a case in which an abnormal course of the branches of the ophthalmic artery led to free arterial bleeding, and in which a subsequent *post-mortem* examination showed that the lacrymal and frontal arteries were derived by a common stem from the middle meningeal, sums up the literature of the subject and enumerates the possible varieties. There is, however, no mention made of the morphology. In view of the conditions found in the animals now under discussion, the occasional origin of the ophthalmic artery, or of some of its branches, from the middle meningeal may be of morphological importance.

Veins.—Whilst the arterial anastomoses in man are few and probably insignificant, the venous anastomoses are large and of great physiological importance throughout the mammalia. Even here, however, a fundamental difference is observed phylogenetically, for in the lower types—*e. g.* the dog (*v. infra*)—most of the blood from the eye is returned to the extra-cranial venous system, while in man it normally passes into the intra-cranial system by way of the cavernous sinus.

Dog.—The blood from the interior of the eye is mainly carried off by the vorticose veins, a small quantity also escaping through the anterior ciliary veins and the central vein of the retina. The vorticose veins are generally four in number, which ultimately unite to form two main trunks. The inferior and external one joins the ophthalmo-cerebral or inferior ophthalmic vein. The superior and mesial trunk runs into the cerebro-facial or superior ophthalmic vein. The two ophthalmic veins communicate with each other in the back part of the orbit, and run into the cavernous sinus. The inferior one usually also communicates with the tributaries of the internal maxillary vein. Both

veins receive numerous tributaries from all the structures in the orbit. The superior vein at the inner canthus joins the nasal veins and becomes the superficial facial. The inferior vein runs under the external wall of the orbit, and at the anterior border of the masseter joins the superficial facial to form the common facial trunk.

Man.—In man the venous anastomoses are free (*see* Quain's 'Anatomy,' Fig. 406). The larger, superior, ophthalmic vein makes a wide communication with the angular vein at the root of the nose, thus entering into relationship with the venous network upon the face,
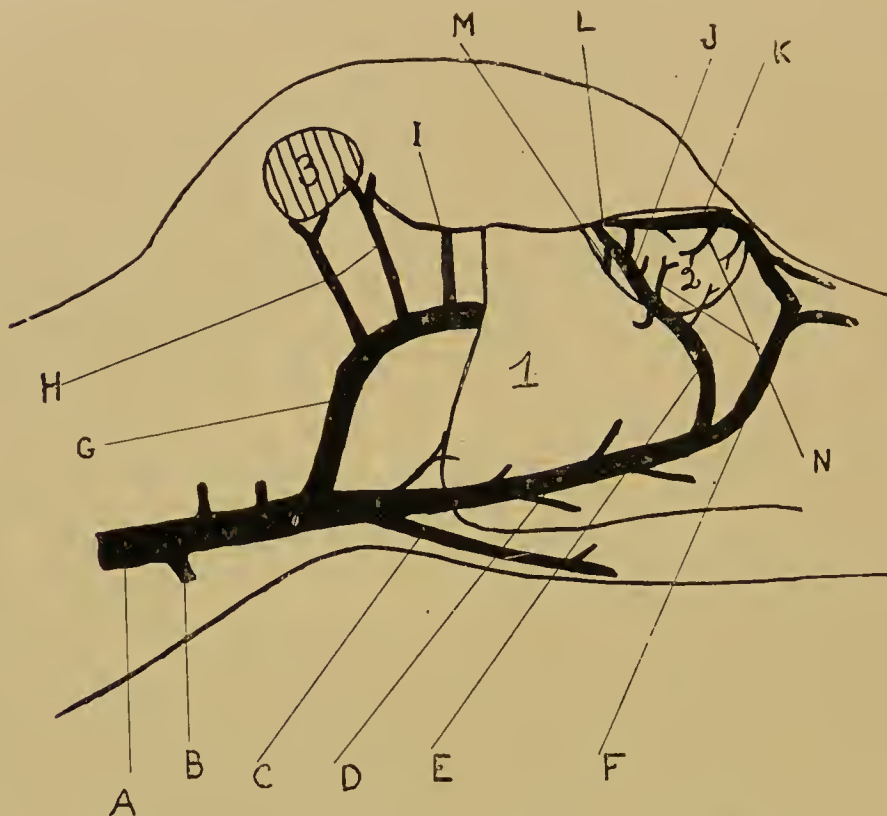
FIG. 674.—SCHEME OF THE EXTERNAL JUGULAR AND OPHTHALMIC VEINS IN THE DOG.

Henderson, R. L. O. H. Rep.. xv. The eyeball, margin of the orbit, and masseter have been removed. A. External jugular vein. B. Communication to external jugular of the opposite side. C. Lingual. D. Common facial. E. Deep facial. F. Superficial facial. G. Internal maxillary. H. Auricular. I. To lateral sinus. J. *Inferior ophthalmic or ophthalmo-cerebral vein.* K. *Superior ophthalmic or cerebro-facial vein.* L. To cavernous sinus. M. To infra-orbital vein. N. Vorticose veins. 1. Placed on the inferior maxilla. 2. On the floor of the orbit. 3. On the ear.

whilst the smaller, inferior, ophthalmic vein communicates with the pterygoid plexus.

KRAUSE.—Die Anatomie des Kaninchens., Leipzig, 1868. ELLENBERGER AND BAUM. —Anatomie des Hundes., Berlin, 1891. F. MEYER.—Morphologisches Jahrbuch, 1887. *HENDERSON.—R. L. O. H. Rep., xv, 1903. *PARSONS.—The Ocular Circulation, London, 1903.

The intra=ocular vessels.—The arrangement of the intra-ocular vessels is somewhat atypical, and demands more detailed description owing to its important physiological and pathological bearings.

The optic nerve.—The intra-cranial portion of the optic nerve is supplied by perforating blood-vessels from the pia mater, like other parts of the brain. The same occurs in the intra-orbital portion, but the supply is here reinforced by small inconstant twigs from the dural sheath, derived from the ophthalmic artery and vein and their branches. The vessels here form networks in each sheath, the meshes of which are elongated in the direction of the course of the nerve. Before the entry of the central vessels of the retina into the nerve, 15—20 mm. from the globe in man, but usually close to the sclerotic in lower mammals, with the exception of monkeys, the nerve is supplied entirely by perforating branches from these networks, which intercommunicate. After the central vessels have entered, they also contribute branches
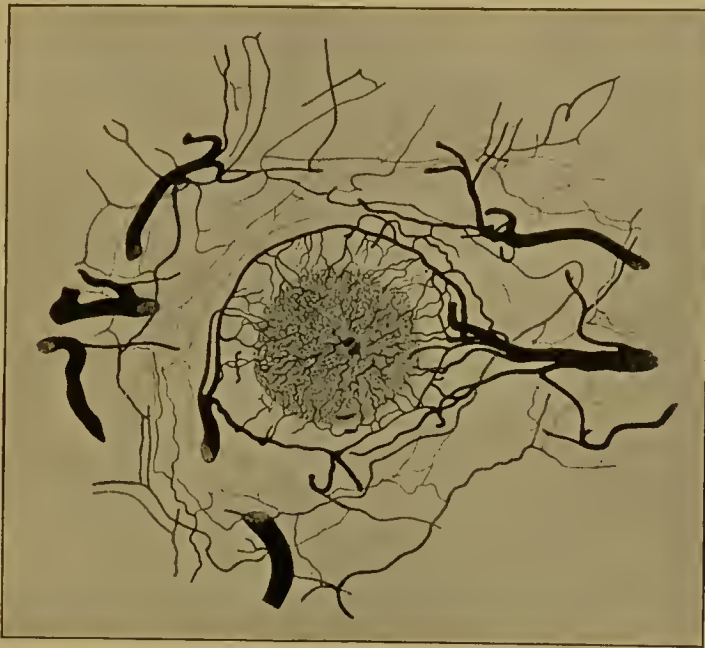
Fig. 675.—Circulus Arteriosus Nervi Optici or Circle of Zinn.
After Leber. Optic nerve and sclerotic injected, retina and choroid removed; arteries black, veins paler. The central artery and vein of the retina are seen in section in the centre of the nerve; at the periphery are several large short posterior ciliary vessels; surrounding the nerve is the circle of Zinn. Note the relative size of the short posterior ciliary arteries and veins.

which anastomose freely with the others. All the vessels run in the supporting connective-tissue framework of the nerve, and hence the reticulum conforms to the distribution of these partitions. This is clearly exemplified by the change which occurs when the lamina cribrosa is reached, the vessels here being smaller and more numerous, and the meshes closer and transversely elongated, whereas they were formerly more open, consisting of larger vessels running longitudinally with transverse and oblique anastomoses. At the lamina cribrosa the vessels are not only derived from the sclera, representing the dural supply, but also from the choroidal vessels. Anterior to the lamina cribrosa, in the intra-ocular end of the nerve, the network again becomes more open, with rounder meshes.

The pial sheath ends at the level of the lamina cribrosa. Its contribution to the blood supply of the nerve is represented farther forwards by the *circulus arteriosus nervi optici*, or *circle of Zinn*. Two or three of the short posterior ciliary arteries are given off at the sides of the optic nerve, and form a ring by the anastomosis of their branches in the sclerotic, just external to the nerve (Fig. 675). Small twigs are given off from this ring to the nerve, and others run back to anastomose with the network of the pial sheath. These vessels apparently have no corresponding veins, and they are further of interest in that they afford an indirect anastomosis between the choroidal and the retinal vascular systems.

There is also a direct anastomosis constantly present between these sets of vessels in this neighbourhood, for both arteries and veins are given off from the choroidal vessels to the nerve-head, and communicate with those derived from the central vessels of the retina (Fig. 676). This anastomosis is limited normally to the nerve-head, and, as is well known, it is only exceptionally that any visible cilio-retinal artery can be seen ophthalmoscopically (*v.* p. 865).

This duplex, direct and indirect, anastomosis between the ciliary and retinal vascular systems in the vicinity of the optic disc is the only communication which occurs normally between them. Elsewhere, as at the ora serrata,

FIG. 676.—DIRECT ANASTOMOSIS BETWEEN THE VESSELS OF THE CHOROID AND THE OPTIC NERVE.

After Leber. The choroid is to the right, the optic nerve to the left; the capillary network is only partially filled in.

they are completely separate. Even these posterior anastomoses are vessels of little more than capillary dimensions, and must be regarded as of relatively small importance under physiological conditions.

The vitreous.—In most adult mammals the vitreous is normally free from blood-vessels. In the embryo the central artery of the retina is continued forwards through the vitreous as the *hyaloid artery*, to supply the posterior vascular sheath of the lens. This vessel occasionally persists as a congenital anomaly, either as a functional blood-carrying vessel, as a short pulsating cæcal vessel filled with blood, as a bloodless, trumpet-shaped process, with its base attached to the disc, or as a fibrous cord stretching for a varying distance into the vitreous (*v.* p. 851). It is found normally in a very rudimentary condition in all ruminants (*e. g.* ox) and in many rodents (*e. g.* guinea-pig).

In all birds, many reptiles, and some mammals, a special vascular organ, the *pecten*, is found projecting from the disc into the vitreous. Structurally it is homologous with the ciliary processes, consisting of a vascular plexus covered by pigmented cells, and it is probably analogous to them in function as a secreting organ. It occurs in its most complicated form in birds (Fig. 677), but it varies enormously in shape in various animals, being most rudimentary in rodents (*e. g.* agoutis) and marsupials. Amongst the latter, the form found in the rat kangaroo (*Hypsiprymnus rufescens*), the rabbit-eared perameles (*Perameles lagotis*),

etc., is approximated in rare cases in man. These cases, however, are probably not vestigial, but pathological new-formed vessels.

In elasmobranchs the vitreous itself is vascularised from a *processus falciformis*. In all holostean fishes and those teleosteans which have no processus falciformis, and in most reptiles which have no pecten, there is a network of vessels upon the hyaloid membrane. In the frog, for example, the circulation of the blood can be observed ophthalmoscopically. The main vessels do not enter by the optic nerve, but behind the insertion of the superior rectus, passing downwards over the disc.

The retina.—The retina is entirely devoid of vessels in nearly all vertebrates except mammals. Other exceptions hitherto recorded are

FIG. 677.—PECTEN OF RHEA.
Section of head of optic nerve, with the pecten attached to it and stretching forward into the vitreous. Note that the retina, seen folded to the left, is devoid of blood-vessels. (I am indebted to the Zoological Society of London for this eye.)

the eel (W. Krause), in which the inner layers are vascularised as far as the inner nuclear layer, and the boa and python (examined ophthalmoscopically by Lindsay Johnson).

Many of the lower mammals—*e.g.* Echidna, Perameles lagotis, Dasypus, Hystrix, Castor, Chinchilla, Myopotamus, Pteropus, Rhinoceros, belonging to the Monotremes, Marsupials, Edentata and Rodentia—are also *anangiotic*.

The vessels are extremely small, extending only over the disc or a short distance from it, in Hyrax, Elephas, Tapirus, Equus, Myrmecophaga, Phalangista, Belideus, Petaurus, Perameles obesula, Hypsiprymnus, Dendrolagus, Capybara, Cælogenys, Cavia—*i. e.* in the majority of Marsupials, Perissodactyls, Edenata, and Rodentia

(Lindsay Johnson).[1] The guinea-pig is a familiar example of the *paurangiotic* retina.

Next come those mammals in which only a portion of the retina has a direct supply, comprising most of the carnivora (especially Felidæ, Viverridæ, Mephitis, Meles, Ursidæ) and some rodents (Sciuridæ, Leporidæ, Myoxidæ). The typical example in this *merangiotic* group is the rabbit, in which the vessels are limited to the horizontal expansion of medullated fibres which is found in this animal (Fig. 686).

In those mammals in which the whole retina has a direct blood-supply—the *holangiotic* group—the lower members have several arteriæ and venæ centrales scattered over the disc, as in the dog (Fig. 678). Others have very elongated discs, with parallel vessels bending over

FIG. 678.—DOG'S RETINA, INJECTED.
From a preparation by Henderson.

the edges (Sciuromorpha); and even multiple discs, each with a central vessel, are found (Cervidæ). The vessels are most centralised in primates.

These variations apparently occur irrespective of phylogenetic position, thus tending to show that specific vascularisation of the retina is not an inherited feature of mammals as a class, but an independent development.

In man the central artery of the retina divides in the middle of the disc, or shortly before it reaches the surface, into a superior and inferior papillary artery, running upwards and downwards respectively. Each of these quickly bifurcates, usually upon the disc, into the superior and inferior temporal and nasal branches. One of the main branches generally gives off a small median artery, running horizontally towards

[1] LINDSAY JOHNSON, 'Phil. Trans.,' B, vol. cxciv, 1902.

the nasal side. The nasal arteries are rather smaller than the temporal, and run radially towards the ora serrata ; whilst the temporal arteries, on the other hand, curve in such a manner as to avoid the macula lutea, sending, however, minute branches towards it. There are also two fine macular arteries, which pass horizontally outwards from the disc, usually arising from the central artery before it has reached the sur- face. The macular vessels break up into capillaries, forming a network around the fovea centralis, which is itself invariably devoid of vessels.

The retinal veins correspond with the arteries, but are more subject to variation, and do not closely accompany the corresponding arteries in their more peripheral course.

The arteries do not anastomose, even as far as their finest divisions, only communicating through the capillary reticulum. There are a
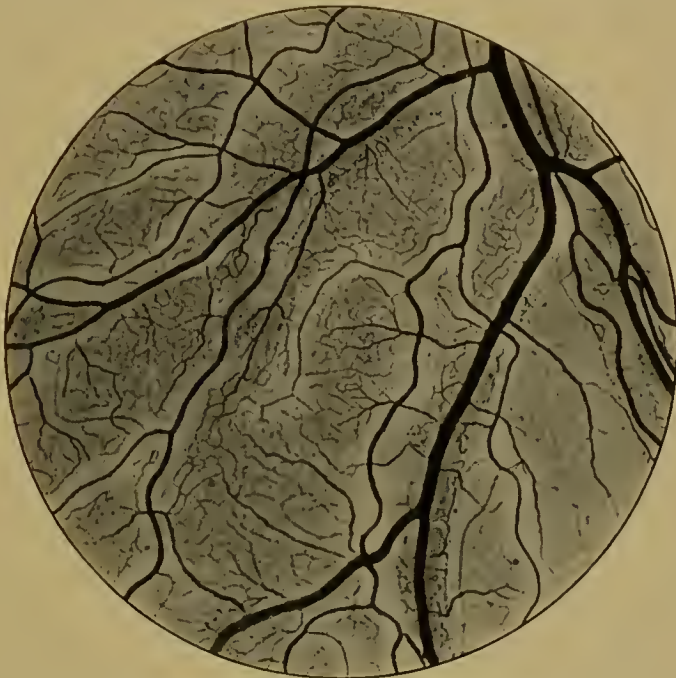
FIG. 679.—DOG'S RETINA, INJECTED.
Higher power, showing perivascular spaces devoid of capillaries.

few small anastomoses of the minute veins near the ora serrata, which, however, are quite unlike the large ring of venous anasto- moses which occurs in this situation in the ox (circulus venosus retinæ anterior).

The retinal venules bend in a circular direction near the ora serrata, but not so the arteries. In the dog the arteries not infrequently bend round and run backwards towards the disc, giving a false impression of recurrent arteries from the ciliary region. As mentioned before, there is no communication with the ciliary vessels at the ora serrata, nor are there any recurrent ciliary vessels to the retina (Fig. 678).

The larger vessels lie immediately external to the internal limiting membrane, which is raised up by them. In a few mammals, e. g. the rabbit, and indeed all the Leporidæ, the vessels are internal to this mem- brane, and cast a distinct shadow ophthalmoscopically.

The capillaries do not extend farther outwards than the external reticular layer, so that the outer nuclear layer, the rods and cones, and the pigment epithelium are dependent for their nourishment upon osmosis from the choroidal or retinal vessels. The capillaries are extremely fine, forming fairly wide meshes (0·02–0·75 mm., Leber). There is an area on each side of the larger vessels which is free from capillaries (Fig. 679); this is occupied in part by the perivascular lymph-sheaths. Since at the fovea centralis the layers of the retina are reduced to such as are elsewhere evascular, so here too there are no vessels, as previously mentioned (Fig. 680).

The uveal tract.—The uveal tract is supplied by the ciliary arteries, which are divided into three groups—the short posterior, the long posterior, and the anterior (Fig. 681). The *short posterior ciliary arteries*, about twenty in number, pierce the sclerotic in a ring around the optic nerve, running almost perpendicularly through the sclera, to which fine branches are given off, as well as to the optic nerve. The *long posterior ciliary arteries*, two in number, pierce the sclerotic slightly farther away from the nerve, in the horizontal meridian, one on the medial, the other on the temporal side. They traverse the sclerotic very obliquely, running in it for a distance of 4 mm. The *anterior ciliary arteries* are derived from the muscular branches of the ophthalmic artery to the four recti. There are usually two from each rectus, with the exception of the rectus externus, which generally supplies only one. They pierce the sclerotic near the limbus, giving off twigs to this region, the conjunctiva and the sclerotic.

FIG. 680.—HUMAN MACULAR REGION, INJECTED.

After Nettleship. The central gap corresponds with the fovea centralis. A. Arteries. v. Veins. N. Nasal side. T. Temporal side.

The ciliary veins also form three groups—the short posterior ciliary, the venæ vorticosæ, and the anterior ciliary. The *short posterior ciliary veins* are unimportant ; they do not receive any blood from the choroid, but only accompany the minute scleral twigs from the posterior ciliary arteries, and are even smaller than the corresponding arteries. The *vorticose veins* are the most important, consisting usually of four large trunks, which open into the ophthalmic vein, or some of the muscular branches. They enter the sclerotic rather behind the equator of the globe, two above and two below. One or more often divides before entry, but there are seldom more than six. They pass very obliquely through the sclera, and often give off smaller branches to the choroid. They also receive blood from the sclera and episclera. The *anterior ciliary veins* are smaller than the corresponding arteries, since they receive blood only from the outer part of the ciliary muscle. There are usually two or three to each rectus muscle.

Of these ciliary vessels, the short posterior ciliary arteries supply the whole of the choroid, being reinforced by recurrent branches from

the ciliary body, which, with the iris, is supplied by the long posterior and anterior ciliary arteries. The blood from the whole of the uveal tract, with the exception of the ciliary muscle, normally leaves the eye by the vorticose veins only.

The short posterior ciliary arteries, on reaching the choroid, run in the outer layers for a distance which varies directly with the situation, posterior or anterior, of their ultimate distribution (Fig. 681). They at first make sharp twists and curves at the posterior pole of the globe, as they lie in the loose pigmented tissue of the suprachoroidea. Passing forwards, they divide dichotomously, the smaller branches invading deeper and deeper the inner layers of the choroid, finally breaking up into the capillary network of the choriocapillaris. The arteries anastomose to some extent at the posterior pole, which is most richly supplied, but less so than the veins. Farther forwards, they do not anastomose *inter se*, but a fresh anastomosis occurs in the anterior parts with the *recurrent ciliary arteries* (Fig. 681). These are generally ten or twelve in number, and are derived from the anterior and long posterior ciliary arteries in the ciliary body. The meshes of the capillary network are fine and polygonal near the optic nerve, but become more and more elongated farther forwards, whilst the capillaries also increase in diameter. There is no relationship between the size of the capillaries and the width of the meshes and the size of the eye in various animals (Sömmering).

The two long posterior ciliary arteries pass forwards between the choroid and the sclerotic, without dividing, as far as the posterior part of the ciliary body. Here each divides into two branches, the bifurcation having an angle of about 45°. They run forwards in the substance of the ciliary muscle, and at its anterior part bend around in a circular direction, anastomosing with each other, and thus forming the *circulus arteriosus iridis major*. This is reinforced by branches from
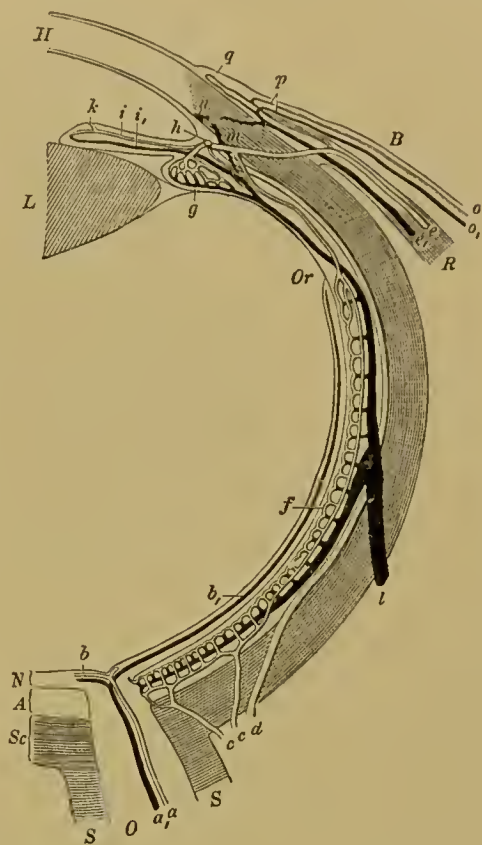
FIG. 681.—SCHEME OF OCULAR BLOOD-VESSELS.

From Fuchs, after Leber. *a.* Arteria centralis retinæ. a_1. Vena centralis retinæ. *b.* Retinal arteries. b_1. Retinal veins. *c.c.* Posterior short ciliary arteries. *d.* Posterior long ciliary arteries. *e.* Anterior ciliary arteries. *f.* Choroidal capillaries. *g.* Capillaries of ciliary body. *h.* Circulus arteriosus iridis major. *i.* Arteries of iris. *k.* Circulus arteriosus iridis minor. i_1. Veins of iris. *l.* Venæ vorticosæ. *m.* Veins from ciliary muscle. e_1. Anterior ciliary veins. *o, o_1.* Posterior conjunctival vessels. *p.* Anterior conjunctival vessels. *q.* Marginal loops of cornea. *O.* Optic nerve. *S.* Its sheath. *Sc.* Sclera. *A.* Choroid. *N.* Retina. *L.* Lens. *H.* Cornea. *R.* Internal rectus. *B.* Conjunctiva.

the anterior ciliary arteries, which also assist in supplying the triangular area left by the bifurcation of the posterior vessels. The arteries break up into a dense meshwork of capillaries, which pervade the ciliary muscle.

FIG. 682.

FIG. 683.

FIGS. 682 AND 683.—VESSELS OF THE HUMAN UVEAL TRACT, INJECTED, FROM THE OPTIC DISC TO THE EDGE OF THE IRIS.

After Leber. Two vorticose veins and their branches are seen. Running up the centre is a long posterior ciliary artery. The capillaries are only partially filled in. Arteries, black; veins, paler.

The circulus arteriosus iridis major is situated in man in the ciliary body at the base of the iris, in many lower animals—*c. g.* the rabbit, in which the ciliary processes invade the back of the iris—it lies in the iris

itself. From it are supplied the ciliary processes and the iris. A
branch from the circle may supply only one ciliary process, or break up
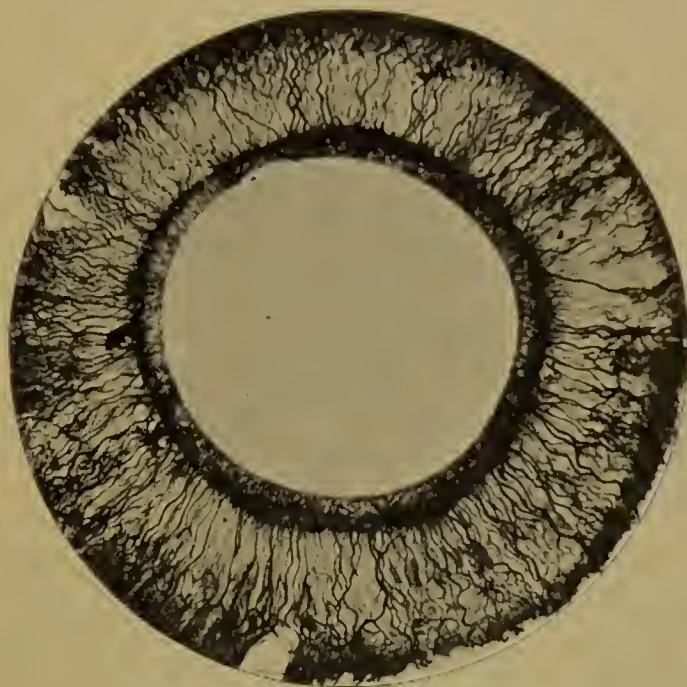
FIG. 684.—HUMAN IRIS, INJECTED.
From a preparation by Nettleship.
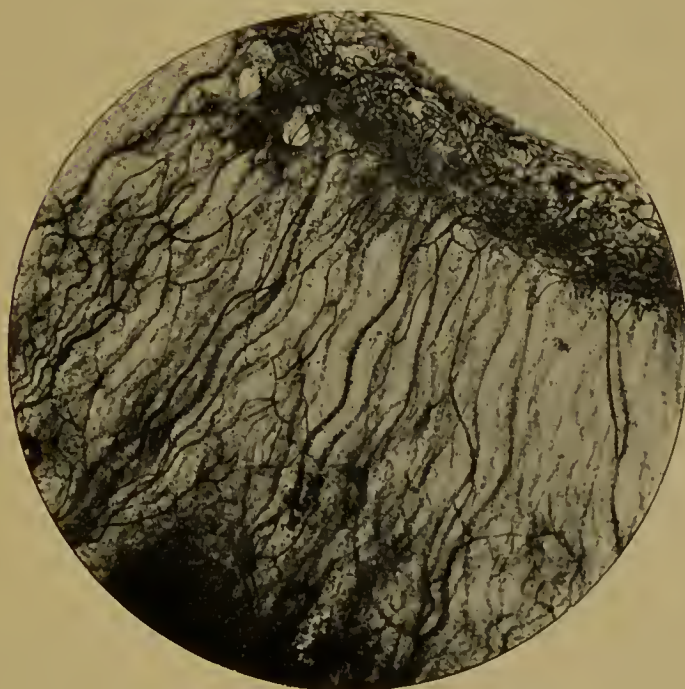
FIG. 685.—HUMAN IRIS, INJECTED.
From the same specimen; higher power.

into two or three, for an equal number of processes. It is to be noted
that these vessels must run through the ciliary muscle in order to reach

the processes, which are, therefore, supplied from in front. The artery of each process breaks up into many anastomosing arterioles, which then form a very rich capillary network, the ciliary processes, in fact, consisting of little more than a dense bunch of vessels.

Other branches from the major arterial circle run radially through the iris, dividing dendritically, and ending in loops at the pupillary edge (Figs. 684 and 685). These iridic arteries are unusually thick-walled in the adult, and difficult to inject. A circular anastomosis takes place a little outside the pupillary margin, the *circulus arteriosus iridis minor*. This marks the place of origin of the fœtal pupillary membrane, and is only developed after the latter has disappeared

Fig. 686.—Albino Rabbit's Retina and Choroid, injected.
From a preparation by Henderson. Note the retinal vessels, limited to the horizontal expansion of medullated fibres.

(Arnold). The capillaries of the iris have a very open network, except those of the sphincter iridis.

The whole of the venous blood from the choroid leaves the eye by the vorticose veins. No veins pass from the choroid with either the short or long posterior ciliary vessels. The tributaries of the vorticose veins are arranged radially, the radii being bent, so as to give a whorled appearance (Fig. 683). The capillaries joining to form the venules in the choriocapillaris also form whorls, called the *stars of Winslow*, though this arrangement is not so marked as in the case of animals which possess a tapetum. The veins from the front and back are naturally the longest, and the posterior branches of neighbouring vortices anastomose, forming U-shaped curves over half the distance from the disc to the equator. The veins from the anterior half of this

distance, in the area between two vortices, pass back into these anastomoses and not directly into the vortices (Fig. 683).

The veins of the iris are gathered together into radial bundles which correspond more or less with the ciliary processes. They pass backwards through the ciliary body, lying towards the inner surface. Here they are joined by the large branches coming from the ciliary processes, and by smaller ones from the ciliary muscle. The whole are gathered together into an immense number of veins running backwards, parallel to each other, through the smooth posterior part of the ciliary body. After reaching the choroid they gradually converge, and unite to form the larger anterior tributaries of the vorticose veins.
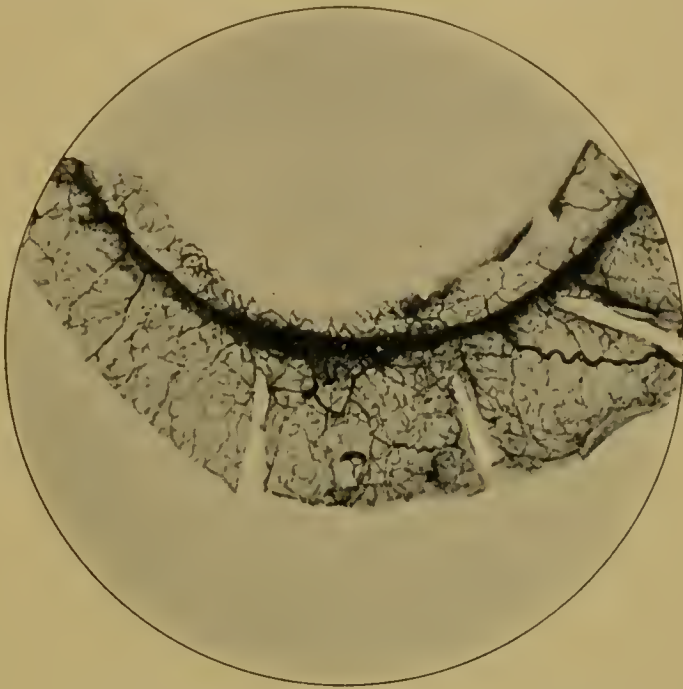
FIG. 687.—HUMAN CONJUNCTIVA, INJECTED.
From a preparation by Nettleship.

In most mammals which have been examined (ox, sheep, horse, pig, dog, rabbit, etc.) there is a large anterior choroidal venous anastomosis, the *circulus venosus Hovii*, into which the veins from the iris and ciliary body open.

The veins from the outer part of the ciliary muscle do not pass backwards with the others, but forwards to become connected with the *circulus venosus ciliaris* or *canal of Schlemm*. This is in reality a plexus of veins forming a ring in the anterior part of the sclerotic, just outside the ligamentum pectinatum iridis. The plexiform nature is most marked where it is joined by anastomoses from the veins of the ciliary muscle. Efferent veins pass from this plexus through the sclerotic to anastomose with the veins from the sclera and episclera, finally joining the anterior ciliary veins, which run with the corresponding arteries. Upon the plexus of the canal of Schlemm and its efferent anastomoses devolves the important function of carrying away the major part of the lymph

from the eye, draining particularly that large lymph-space, the anterior chamber.

Branches of the anterior ciliary arteries, after giving off the anterior conjunctival arteries, break up dichotomously into excessively fine vessels, which anastomose freely with each other, and end in minute loops at the edge of the cornea. These invade the cornea for a very short distance only—1-1½ mm. above and below, ½-1 mm. at the sides —the remainder being free from vessels (Figs. 687 and 688), a fact which is true also of the cornea throughout fœtal life (Leber, Schöbl, Hirsch).

The anterior conjunctival vessels are also given off from the anterior ciliaries, not far from the corneal margin. They form a superficial
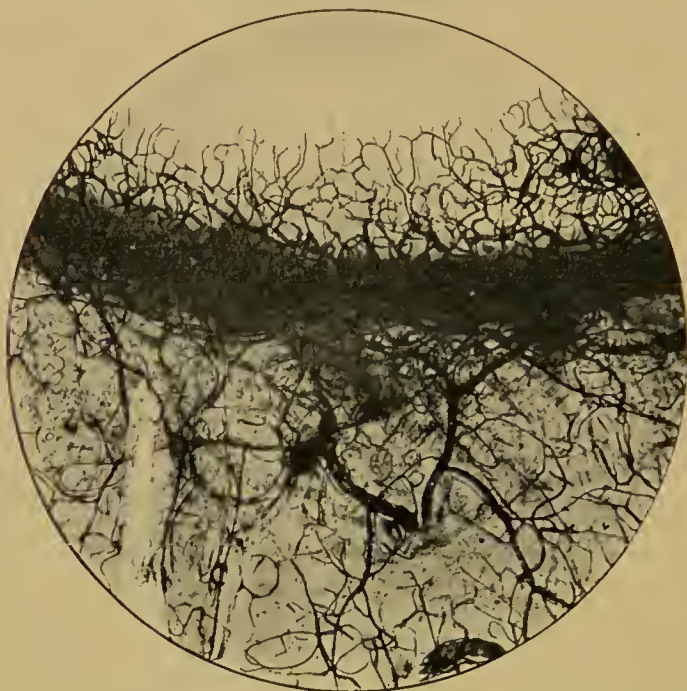
Fig. 688.—Human Conjunctiva, injected.
Showing corneal marginal loops. Higher power.

group of vessels, and run backwards in a radial direction immediately after their origin, and finally contribute to the loose capillary network of the conjunctiva. The anastomosis which occurs between the more superficial, conjunctival, and the deeper, episcleral, vessels increases from behind forwards, being richest at the limbus, a fact which is demonstrated so often clinically.

*Leber.—Denkschrift d. k. Akad. der Wiss. zu Wien. Math.-naturwiss. Cl., xxiv, 1865 : in G.-S., ii, 1900 (Bibliography).

The lymphatic system.—There are no typical lymphatic vessels within the eye ; these only occur in the conjunctiva. Some of the vessels which perforate the sclerotic and some of those within the eye, e. g. the retinal vessels, possess perivascular adventitial lymph-spaces ; otherwise the lymph is contained in intercellular spaces and clefts, or

in larger lymph-reservoirs. The most important of the latter are the anterior and posterior chambers, the spaces of the zonule of Zinn, the central canal of the vitreous or Cloquet's canal, the perichoroidal space, Tenon's capsule, and the intervaginal space of the optic nerve. The intra-ocular lymph-spaces may be regarded as extensions of the intra-cranial lymphatic system, the subarachnoid space being continued forwards, little changed in the optic nerve, then reduced to a potential space, the perichoroidal, and finally expanded into a large reservoir, the anterior chamber, the ligamentum pectinatum of which shows a marked resemblance to the subarachnoid meshwork (Leber).

The minute anatomy of these lymph-spaces has been described in Part I. There are some points of physiological importance which cannot be demonstrated by purely anatomical methods. It will be necessary to refer to these briefly here.

There is no direct communication between the anterior chamber and the canal of Schlemm, as was at one time held by Schwalbe (v. infra), neither are there any lymphatic vessels draining the anterior chamber. Thus, if coloured solutions are injected into the anterior chamber, they pass out solely by way of the anterior ciliary veins (Schwalbe, Leber). If the blood-vessels are previously filled with a gelatine mass, so that this means of exit is cut off, injection of solutions into the anterior chamber still fails to reveal lymph-vessels. According to Schwalbe the anterior ciliary veins have no perivascular lymph-spaces (v. infra).

Injections of Indian ink, etc., into the anterior chamber pass also into the posterior chamber and into the canal of Petit, which is proved by these and other experiments not to be a closed canal, but merely a system of spaces between the fibres of the suspensory ligament. The mass also passes for a short distance behind the lens, but is prevented from passing completely round it by the firm adhesion of the lens to the patellar fossa. In the case of Indian ink, some of the particles are found in the vitreous, and, indeed, become so closely aggregated upon the very delicate hyaloid membrane that it appears uniformly black; later the particles become diffused between the vitreous fibrillæ (Leber).

The hyaloid membrane, separating the canal of Petit from the vitreous, is readily permeable to fluids by filtration. From the vitreous fluid passes into the canal of Cloquet or Stilling, and thence by very fine perivascular lymph-spaces round the central vessels to the inter-vaginal space. The central canal of the vitreous can be demonstrated by dropping coloured fluid upon the posterior triangular expansion (Stilling), by injection of Berlin blue or alkannin turpentine under the pial sheath of the nerve (Schwalbe), or into the axis of the nerve near the central vessels (Leber). In some cases it becomes marked out with Indian ink after injection of the posterior chamber (Leber).

The perichoroidal space stretches from near the insertion of the ciliary muscle to 4 or 5 mm. from the optic-nerve entrance—i.e. to the zone in which the posterior ciliary vessels and nerves perforate. It is normally a capillary space, lined with endothelium, and is in direct communication with the lymph-spaces in the choroid (Sattler). The

veins only of the choroid are surrounded by perivascular lymph-spaces, and these give exit to the fluid in the spaces between the arteries and capillaries, but not to that in the larger lymph-spaces of the choroid (Sattler). The fluid is carried away from the perichoroidal space by the perivascular lymph-sheaths of the emissaries of the vortex veins, thus communicating with Tenon's capsule. This fact is easily proved by injection of the perichoroidal space (Schwalbe). Anatomically only the inner third of the vortex veins, as they pass through the sclerotic, possess a definite perivascular space, and this is traversed by fibres, which form a kind of mesentery (Fuchs, Birnbacher and Czermak, Langer). The same structure is found around the long and short posterior ciliary arteries and the anterior ciliary arteries and veins (Fuchs), so that all probably possess functional, though somewhat atypical, lymph-sheaths (cf. Schwalbe).

The retinal vessels, like those of the brain, are surrounded by peri-vascular lymph-sheaths. This was first proved by His; by forced injection of the vessels, some of them burst in places, allowing the mass to flow into the sheaths. His succeeded in injecting both vessels and sheaths by different coloured masses. It is doubtful whether the arteries possess perivascular sheaths; they are certainly more difficult to demonstrate. The spaces may also be injected from beneath the inner sheath of the optic nerve (Schwalbe), and the mass then passes out into ray-like clefts in the nerve-fibre layer and between the vitreous and internal limiting membrane, or even into the central canal.

The subarachnoid space is easily injected from the same space around the brain, and it is also in free communication with the subdural space (Schwalbe, Key and Retzius). These, again, communicate by way of the perivascular spaces of the dural sheath with the orbital lymphatics and Tenon's capsule. According to v. Michel the peri-choroidal space communicates with the subarachnoid around the optic nerve, but this is not the case in lower animals (Schwalbe). The lymph-spaces of the optic nerve cannot be injected from the intervaginal space (Schwalbe, Forlanini, Wolfring, v. Michel, Key and Retzius). They are readily demonstrated by injection beneath the pial sheath, the mass flowing between the bundles of nerve-fibres, or even around the individual fibres, according to the pressure of injection. The intra-neural lymphatic system is particularly well-developed in the lamina cribrosa.

The conjunctiva possesses a superficial and a deep network of lymphatic vessels (Teichmann, Schmid, Waldeyer, Fuchs, Klein), and these communicate with each other by short anastomoses. They can be injected either from beneath the conjunctiva or from the cornea. In both cases it is best not to use a watery solution, which causes much swelling and distortion; alkannin turpentine (Leber) and asphalt benzol (Klein) are recommended. The superficial plexus consists of fine, uniform vessels, the deep of coarser, irregular vessels with more valves. There is a very fine network at the limbus. The larger peripheral vessels run parallel to the blood-vessels to the inner and outer angles. Where there are follicles, as in lower animals, these are surrounded by a dense network. The tarsal plexus is finer than that

of the fornices; it communicates with the pretarsal system chiefly at the lid margin, there being few anastomotic vessels passing through the tarsus.

Injection of the cornea demonstrates two kinds of spaces: (1) Bowman's corneal tubes, long spindle-shaped spaces, due to separation of the lamellæ, best shown by injection of air or mercury; these are undoubtedly artefacts; (2) spaces taking the shape and arrangement of the fixed corpuscles and nerves. Both arc usually seen in the same preparation, the first best in the ox, the second in the rabbit (Leber). It is probable that the perineural spaces are true lymph-spaces. According to Leber there are no true lymph-spaces in the cornea, the fluid circulating by diffusion.

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PHYSIOLOGY.

LYMPH-PRODUCTION AND EXCRETION.

The normal aqueous.—The anterior and posterior chambers contain 0·23—0·4 c.c. of aqueous (Krause, Petit, Sappey, v. Jäger, and Kletzinsky); it has a specific gravity of 1008—1009 in lower animals (Golowin, v. Michel and Wagner), but only about 1004 in man (Chenevix, Kletzinsky). It is a clear, alkaline fluid, containing about 1 per cent. of solids (Kletzinsky, Villasenor). Kletzinsky found 0·045 per cent. of proteids; Wessely in rabbits, by an optical method of estimation, 0·02 per cent.; the percentage is therefore extremely low. The proteids are serum albumin and serum globulin. Normal aqueous does not undergo spontaneous coagulation; it contains neither fibrinogen nor fibrin ferment (Jesner).

The aqueous contains traces of grape-sugar (Claude Bernard, Chabbas, Jesner, Leber, 0·045—0·05 per cent.); this has been put beyond dispute by the demonstration of the osazon (Pautz). The amount is generally, but not invariably, increased in diabetes (v. Vol. II, p. 426) (Störer, Knapp and Carius, Goldschmidt, Leber, Deutschmann, and others). Normal aqueous also contains a diastatic ferment, as is shown by digestion with starch solution (Leber). It contains traces of paralactic acid (Grünhagen, Pautz) and urea (Millon, Wöhler, Pautz). The inorganic constituents amount to 0·8—0·9 per cent. in oxen (Lohmeyer, Cahn, v. Michel and Wagner), but only 0·58—0·64 per cent. in man (Kletzinsky); most of this is sodium chloride—about 0·7 per cent. (Lohmeyer, Cahn), 0·48—0·53 per cent. (Kletzinsky). Cahn gives the following analysis of the inorganic constituents of aqueous and vitreous:

		Aqueous.			Vitreous.
Sodium chloride	. .	78·11	.	.	74·43
Sodium carbonate	. .	8·72	.	.	12·67
Potassium chloride	. .	2·92	.	.	5·57
Potassium sulphate	. .	5·99	.	.	3·74
Sodium phosphate	. .	1·99	.	.	1·82
Calcium phosphate	.	0·62	.	.	0·44
Magnesium phosphate	.	0·40	.	.	0·22
		98·75			98·89

The aqueous and vitreous contain free carbonic acid, as is shown by the phenolphthalein test; addition of phenolphthalein solution causes no change in colour; on warming, which drives off the carbonic acid, the mixture turns red; on standing, the colour gradually fades through reabsorption of carbonic acid from the atmosphere. The reaction has been attributed erroneously to a normal acid reaction in the aqueous (Dor), but this can be disproved by the litmus reaction (Mays).

The osmotic coefficient of the aqueous in the ox was found by the lowering of the freezing point to be equivalent to 0·959 per cent. sodium chloride, by the blood-corpuscle method, 0·995 per cent. (Kunst), or 0·981 per cent. (Manca and Deganello). The osmotic coefficient of aqueous compared with that of blood-serum is 11 : 10 (Hamburger, Manca and Deganello).

The aqueous which is secreted immediately after emptying the anterior chamber by a puncture or paracentesis differs from normal aqueous in being spontaneously coagulable, and in containing a greatly increased amount of proteid. Up to three and a half hours the fluid is replaced by a dense coagulum on heating or addition of nitric acid. In the rabbit the fluid does not coagulate spontaneously after four hours, but the normal proportion of proteid is found only after six to eight hours (Bauer). Leber was unable to find leucocytes in the interval from half to twelve hours after paracentesis.

The presence of alexins, etc., in the aqueous will be considered elsewhere.

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The normal vitreous.—The fibrillar tissue of the vitreous, obtained by mincing it up and filtering off the contained fluid, is a collagenous substance yielding glutin on heating for five hours at a temperature of 105° to 108° (Boë, Mörner).

The fluid is almost identical with aqueous; the specific gravity in the ox is about 1007 (1007·6–1008·8, v. Michel and Wagner), in man 1008·9 (Giacosa). The proteids, serum albumin and serum globulin, are present in small quantities as in the aqueous; estimations differ, partly owing to the method employed, mucin being precipitated and reckoned in by some of the methods, partly owing to differences, according to the part of the vitreous investigated (Leber). A mucinous substance was described by Virchow and confirmed by Portes, Boë, and Mörner, who called it "hyalomucoid." It is not easily demonstrated by the usual acetic acid test owing to the large amount of salts present, but is precipitated on dilution with 2–3 volumes of water and addition of acetic acid up to 1 per cent. That it is a true mucin is proved by the liberation of a reducing substance on warming with dilute acids. The quantity is not more than 0·1 per cent. (Mörner). Traces are said to be present in aqueous (Mörner), but this is doubtful (Leber). It is possible that the mucin in the vitreous is derived from amœboid cells (Iwanoff).

Sugar is present (Jesner), a fact placed beyond dispute by the demonstration of the dextrosazon (Pautz); urea can also be easily demonstrated (Millon, Wöhler, Schneyder, Pautz). Paralactic is shown by Uffelmann's reaction, and by other more delicate tests (Pautz). As in the aqueous, there is also a diastatic ferment (Lépine); it is possible that this is due to bacterial contamination (Leber), and Lépine finds that it is not present immediately after death, a fact which he considers due to a non-active precursor or mother-substance. There is no spontaneous coagulation, so that fibrin ferment is probably absent (v. Michel and Wagner).

The inorganic constituents amount to nearly 1 per cent. (Lohmeyer, Cahn, v. Michel and Wagner, Portes), sodium chloride accounting for 0·77 per cent. (Lohmeyer). The proportions of other salts have already been given (v. p. 964).

The osmotic co-efficient is about the same as that of aqueous (Kunst):

	Vitreous. Per cent. NaCl.	Aqueous. Per cent. NaCl.
By the blood-corpuscle method	0·96	0·971
By the freezing-point method	0·925	0·959

The similarity of constitution of aqueous and vitreous is confirmed by the determination of the refractive index, both giving results nearly approximating 1·337 (Helmholtz, Fleischer, Hirschberg, Kunst).

Boë.—Soc. franç. d'O., 1886. Mörner.—Z. f. physiol. Chemie, xviii, 1893. v. Michel and Wagner.—A. f. O., xxxii, 2, 1886. Giacosa.—Arch. per le Sc. med., vi, 1882. Virchow.—Virchow's Archiv, iv, 1852. Portes and Beauregard.—Jl. de l'Anat. et de la Phys., xvi, 1880. Iwanoff.—A. f. O., xi, 1, 1865. Jesner.—Pflüger's Archiv, xxiii, 1880. Pautz.—Z. f. Biol., xxx, 1894. Helmholtz.—Physiologische Optik, 1896. Fleischer.—Dissertation, Jena, 1872. Hirschberg.—A. f. A., iv, 1874. Kunst.—Dissertation, Freiburg, 1895. *Leber.—In G.-S., 1903. (For other references see "The Normal Aqueous.")

Lymph=production.—The normal intra-ocular tension is maintained by keeping the quantity of fluid within the globe constant. As the fluid is continually draining away slowly into the venous system a con-

stant quantity can only be maintained by an equivalent slow renewal of fluid.

Hovius (1702) first attempted to measure the amount of fluid which drained away when the anterior chamber was opened. Jesner found the amount in the rabbit to be 48 c.mm. per minute; since the volume of the rabbit's anterior chamber is about 300 c.mm. the chamber would be refilled in about six minutes. Leplat gives smaller values—7-20 c.mm., results probably vitiated by coagulation. If the drainage is measured against varying pressures it is reduced to *nil* when the pressure is equal to the normal intra-ocular pressure, as might be expected; the amount is inversely proportional, roughly speaking, to the adverse pressure (Adamük, Jesner). Hence it may be concluded that under normal circumstances the whole of the fluid secreted is absorbed into the blood circulation, and further, that the amount secreted cannot be estimated by the amount which will drain off through a cannula.

That constant reabsorption of the fluid secreted is taking place is shown by the injection of an indifferent fluid into the anterior chamber of a freshly removed eye under constant pressure. If a horizontal glass tube containing an air-bubble is interposed between the reservoir of fluid and the eye, it will be seen that the air-bubble moves towards the eye. Moreover, the fluid, especially if it be coloured, can be seen to exude from the cut ends of the anterior ciliary and vortex veins, and the pericorneal region becomes injected with the coloured fluid (Priestley Smith). This method indicates the principles upon which the rate of secretion of the intra-ocular fluid can be measured. For accurate determinations it is necessary to use a specially arranged manometer; as the same arrangement is employed for measuring the intra-ocular pressure, the description of the instrument and its modifications will be considered in that connection (*v. infra*).

The eyes experimented upon must be as fresh as possible, and the fluid well filtered; 0·75 per cent. NaCl solution is used for injection. After connecting the eye with the manometer the fluid runs in rapidly, filling the anterior chamber and the empty blood-vessels. Readings are only to be taken when the movements of the air-bubble become constant. After a considerable time the readings again become untrustworthy owing to blockage of the paths of filtration with suspended particles and to swelling of the tissues.

The following results have been obtained by various observers, using slightly different forms of apparatus, all, however, based upon the same principle. Bentzen and Leber obtained a filtration of 5 c.mm. per minute in the human eye thirteen hours after death at a pressure of 25 mm. Hg.; Niesnamoff, 5·5 c.mm. In the rabbit Bentzen obtained 6 c.mm. and Niesnamoff 7 c.mm. In the sheep's eye Priestley Smith obtained a filtration of 26 c.mm. per minute. Niesnamoff found in the pig 11 c.mm., dog 18 c.mm., cat 24 c.mm., sheep 28 c.mm., ox 62 c.mm. Taking 5 c.mm. as the average filtration per minute in man, and the volume of the anterior chamber as 0·24 c.c. (v. Jäger), the aqueous will be renewed in about forty-eight minutes. In the rabbit, with a filtration of 7 c.mm. and a volume of 0·3 c.c. (Bellarminoff), the aqueous will be renewed in about forty-three minutes. It is evident, therefore, that

the renewal of fluid is extremely slow, so that there is no question of a flow or current of fluid through the anterior chamber. Many other observations confirm this point—*e. g.* the behaviour of cholesterin crystals and other suspended particles in the anterior chamber. Such particles move entirely and solely in accordance with their specific gravity—*e. g.* the leucocytes in hypopyon, the precipitates in "keratitis punctata," etc. Similarly particles of gold-leaf introduced into the anterior chamber of a rabbit move up and down in circular paths in front of the iris and pupil, finally becoming deposited upon the iris (Leber). If fluorescein is injected subcutaneously or intraveneously it appears in the anterior chamber as a vertical line, the so-called Ehrlich's line ; this, contrary to Ehrlich's explanation, is due to the specific gravity of the fluorescein solution (Leber) (*v. infra*).

The experiments of Adamük, Jesner, and Niesnamoff show that the amount of fluid secreted is proportional to the difference in pressure within the blood-vessels and that within the eye, *i. e.* outside the vessels. In other words, the secretion follows the physical laws of filtration and is not a true physiological "secretion." If the cannula of a filtration manometer is introduced into the eye the conditions vary according to the difference between the intra-ocular and manometric pressures. If these are the same no fluid enters or leaves the manometer. If the manometer fluid is at a higher pressure than the eye fluid flows from the manometer into the eye. The quantity which enters the eye is less than that which enters the excised eye under similar conditions, because fluid is being secreted by the eye itself. Hence the difference between the amounts of fluid entering the living and the dead eye will give the amount of fluid secreted by the eye at the given pressure. If the pressure in the apparatus is less than that in the eye fluid will flow into the manometer.

Niesnamoff found that the amount of fluid secreted for each mm. Hg pressure is nearly constant ; this is called the *filtration co-efficient.* The filtration at any given pressure is therefore obtained by multiplying the pressure by the co-efficient of filtration. The co-efficient of filtration is different for different animals : Man 0·215 c.mm., rabbit 0·275 c.mm., pig 0·440 c.mm., dog 0·720 c.mm., cat 0·960 c.mm., sheep 1·120 c.mm., ox 2·480 c.mm. The *secretion co-efficient* can be determined similarly ; thus in the rabbit at 25, 33, and 48 mm. Hg for every increase of 8 mm. Hg the secretion diminishes by 2 c.mm.—*i. e.* 0·25 c.mm. for each mm. Hg. Hence the diminution of secretion is proportional to the increase of pressure, and 0·25 is the co-efficient of secretion. When the pressure reaches 50 mm. Hg in the rabbit—*i. e.* about twice the normal intra-ocular pressure—secretion ceases ; this, therefore, gives the intra-vascular pressure. Grönholm, by injection into the vitreous, found that secretion was not quite abolished at 50 mm. Hg.

It is doubtful whether the relationship of secretion and filtration to intra-ocular pressure is quite so mathematically accurate as would be deduced from Niesnamoff's experiments.

If the production of intra-ocular fluid is dependent on a process of filtration through the blood-vessels and the epithelium covering the ciliary processes, its rate must vary directly with the difference of

pressure on the two sides of the filtering membrane. It must vary, therefore, directly with changes in the capillary blood-pressure, and inversely with the changes in the intra-ocular pressure. Henderson and Starling sought to eliminate the second factor, namely that of absorption, by opening the anterior chamber, so that the intra-ocular pressure could be regarded as zero. A cannula was introduced into the anterior chamber and the fluid allowed to flow off into weighed porcelain capsules. These were changed every ten or twenty minutes, and the amount of fluid secreted in the time determined by weighing. The fluid drained off during the first minute after insertion of the cannula was regarded as normal intra-ocular fluid, but the gradual emptying of the eye-ball continues during the first five minutes, so that the figures obtained during this time cannot be regarded as expressing the rate of secretion. In every case the total solids of the intra-ocular fluid were also determined.

Cat, anæsthetised with Ether and the A.C.E. Mixture. A small Dose of Curare was injected after Anæsthesia was complete. The Extract of 2 Grammes of dried Leech Heads was injected.

Time.	B.P. in mm. Hg.	Weight of secretion.	Weight of solids after drying to a constant weight.	Percentage of solids.	Rate of flow per minute.
		grammes.	grammes.		grammes.
3.50 cannula inserted.					
3.51	130	0·689	0·009	1·3	—
3.56	145	0·252	0·007	2·7	0·05
4.16	120	0·756	0·032	4·2	0·037
4.36	100	0·475	0·021	4·4	0·023
4.56	96	0·482	0·024	4·9	0·024

The above experiment shows the results obtained while the blood-pressure was approximately constant. It will be seen that there is a constant diminution in the amount of fluid obtained. These experiments are complicated by the formation in the anterior chamber of clots, which tended to plug the cannula. This difficulty could be obviated by the injection of a dose of leech extract, not large enough to cause a permanent diminution of the blood-pressure.

The next question to determine was whether it was possible to alter the rate of production or the composition of the intra-ocular fluid by altering the blood-pressure in the vessels of the eyeball. Experiments on this point were all carried out on dogs (Henderson and Starling). A diminution of the intra-ocular blood-pressure was easily effected by ligature or obstruction of the carotid artery on the same side. In order to produce a maximal rise of pressure in the blood-vessels of one eye, the vertebral and subclavian arteries on both sides were tied. A loose ligature was placed round the thoracic aorta, so as to permit of its

being obstructed at any given time. A cannula connected to the mercurial manometer was placed in the carotid artery on the right side. The production of intra-ocular fluid was determined in the left eye. By obstruction of the aorta a large rise of blood-pressure was produced in this eye, since all the blood had to pass through the one carotid artery in order to get back to the heart. On the other hand, an almost complete anæmia could be produced in the eye by obstruction of the one remaining carotid. Below are the results of one such experiment.

Dog. Weight, 7½ Kilos. Anæsthetised with the A.C.E. Mixture and Morphia. The extract of 2 Grammes of dried Leech Heads was injected. Both Subclavians and Vertebrals were tied. Temporary Ligature round Aorta. Cannula in left Eye. B.P. observed in right Carotid.

Time.	B.P. in mm. Hg.	Amount of secretion in grammes.	Total solids in grammes.	Percentage of solids.	Rate of flow.	Remarks.
3.29	—	—	—	—	—	Cannula inserted. Aorta unobstructed.
3.30	110	0·811	0·C13	1·5	—	—
3.35	110	0·432	0·014	3·2	0·086	—
3.45	100	0·550	0·027	4·9	0·055	—
3.55	205	1·153	0·068	5·9	0·115	Aorta obstructed. Fluid tinged red
4.5	100	0·627	0·039	6·2	0·062	Aorta unobstructed.
4.15	198	0·816	0·053	6·6	0·081	Aorta obstructed.

It will be seen that in every case a rise of intra-ocular pressure caused an increase in the amount of fluid secreted. It is impossible, however, to deduce directly from these experiments that the intra-ocular fluid is a transudation. The opening of the eye-ball and the consequent diminution of the intra-ocular pressure to zero have a serious effect on all the intra-ocular structures. Great dilatation of the vessels of the ciliary processes and iris is produced. The fluid, which, in the normal eye, is free from fibrinogen and contains the merest trace of proteid, rapidly acquires the power of coagulation, and its proteid content rises to 3, 4, or 5 per cent. The serious alteration of the vascular structures is shown in many cases by the appearance of red blood corpuscles in the fluid dropping from the cannula, and Greeff has shown that if the lowered pressure be brought about suddenly and maintained for some time, the epithelium covering the ciliary processes may be raised from the surrounding tissue so as to form small blisters, which are filled with coagulable lymph. It has been suggested by Greeff that the change in composition of the intra-ocular fluid ensuing on opening the eye-ball is determined by the separation of the epithelium; but Bauer has shown that the proteid content may be raised in the absence of these epithelial changes, and that, on the other hand, the epithelial changes may be well marked on the subsequent day, when the wound

in the cornea has closed, and the intra-ocular fluid has regained its normal composition. He also points out that the amount of change produced depends entirely on the rapidity with which the intra-ocular pressure is lowered. The change in composition is probably due, as Leber suggests, to the great distension of the capillaries and the consequent separation of their epithelial cells. It represents, in fact, an alteration in permeability of the filtering membrane.

Amount of intra-ocular fluid produced under normal circumstances.—In any investigation of the factors determining the production and absorption of intra-ocular fluid it is important to get some idea of the amount of this fluid secreted under normal circumstances—that is, at normal intra-ocular pressure. Since the intra-ocular pressure is maintained constant so long as the blood-pressure is steady, the amount of fluid produced at a given intra-ocular pressure must be equal to the amount of fluid absorbed at the same pressure. It is, therefore, a matter of indifference whether the amount formed or the amount absorbed at any given pressure is measured. Leplat sought to abolish the absorption of the intra-ocular fluid by filling the anterior chamber with oil or vaseline. A cannula was placed in the vitreous cavity, and the pressure in the cannula maintained at the normal intra-ocular pressure. It was found that the obstruction of the absorbing angle of the eye-ball carried out in this way caused a rise of intra-ocular pressure if the eye-ball were closed, or a flow outwards of intra-ocular fluid by the cannula if the pressure in this was maintained at the normal intra-ocular pressure. The amount of this outflow was measured, and was regarded by Leplat as representing the normal rate of formation of intra-ocular fluid. He arrived at the conclusion that the amount of fluid normally secreted by the ciliary processes is in the rabbit about 4 c.mm. per minute. There are considerable difficulties in applying this method, chiefly determined by the tendency of the cannula in the vitreous to become blocked. Henderson and Starling therefore adopted a method similar to that already employed by Niesnamoff under Leber's direction. The arrangement of the experiment was as follows:

The hollow needle, connected by the capillary tube (containing an air bubble as index) to the reservoir and manometer, was introduced into the anterior chamber. The height of the reservoir was then adjusted until the bubble was stationary, showing that the intra-ocular pressure was exactly balanced by the pressure of the fluid in the tube leading to the reservoir. This intra-ocular pressure was, of course, maintained by a constant secretion of intra-ocular fluid, exactly equal to the amount escaping by filtration through the anterior angle of the eye. The animal was then killed by dividing the heart. This procedure at once stopped the production of intra-ocular fluid. The intra-ocular pressure, however, was maintained at its previous height by the connection of the eye with the reservoir of Ringer's fluid; the escape of fluid by the anterior angle was, therefore, the same as before. The rate of this escape could be determined by noting the rapidity with which the air bubble moved along the capillary tube toward the eye, and this rate must be equal to the rate of *production* of fluid previously obtaining in the eye under normal conditions of circulation. The

following table gives the rate of production of intra-ocular fluid, determined in this way, with varying intra-ocular pressures :

Animal.	Intra-ocular pressure in mm. Hg.	Inflow, after cessation of circulation, in cubic millimetres per minute.
Cat . . .	20	12
Cat . . .	15	11
Cat . . .	26	12
Cat . . .	28	10
Cat . . .	14	5
Cat . . .	20	15
Average .	20.5	10.8

It will be seen that there is a considerable difference in the case of filtration in various eyes, and therefore a corresponding difference in rate of production of intra-ocular fluid.

In another set of experiments Henderson and Starling determined the rate of absorption of intra-ocular fluid at the normal intra-ocular pressure, and regarded this as representing the rate of production of this fluid under normal circumstances. In the same experiment it was possible to alter the intra-ocular pressure by raising or lowering the reservoir, and so to determine the effect of the height of the intra-ocular pressure on the rate of absorption. The results of two such experiments are given below, and show conclusively that the rate of absorption is determined, in the absence of disturbing factors which we shall have to consider later on, solely by the height of intra-ocular pressure :

(1) *Cat, anæsthetised with Ether. While the Anæsthesia was maintained, a small Dose of Morphia and Curare was injected. Atropin was instilled locally into the Conjunctival Sac.*

B.P. in mm. Hg.	I.O.P. in mm. Hg.	Rate of inflow in cubic millimetres per minute.
115	22	0
115	30	4
115	46	7
130	62	8
Heart divided.		
0	22	12
0	36	16
0	46	19
0	62	22

(2) *Cat, anæsthetised with Ether. Atropin and Cocain instilled locally into the Conjunctival Sac.*

B.P. in mm. Hg.	I.O.P. in mm. Hg.	Rate of inflow in cubic millimetres per minute.
124	32	0
124	44	5
124	52	11
110	20	0
116	44	10
116	52	20
	Heart divided.	
0	52	22
0	44	15
0	20	12

The intra-ocular pressure varies directly as the blood-pressure in the vessels of the eyeball (*v. infra*). It must, therefore, be concluded that the rate of absorption of intra-ocular fluid is also determined by the height of the blood-pressure, and since the absorption must keep pace exactly with the formation of this fluid, it follows that the formation of the intra-ocular fluid must also be determined by the height of the intra-ocular blood-pressure. So far, then, the conditions laid down as necessary to be fulfilled in order to justify the filtration theory of the production of intra-ocular fluid have been fulfilled, and it might be concluded with Leber that the formation of this fluid is exactly analogous to that of lymph, and is determined by the difference of pressure between the blood in the vessels and the fluid outside the vessels. There are, however, certain difficulties in this assumption which have not so far been considered by previous workers, but which must be met satisfactorily before any definite conclusion on the subject can be arrived at.

It has hitherto been assumed by Leber, Niesnamoff, and others, that a fluid having the composition of intra-ocular fluid might be formed by a process of filtration through the blood-vessels of the ciliary processes under any difference of pressure. In this assumption they have neglected the question of the different proteid content of blood-plasma and intra-ocular fluid. Starling has shown that, in order to separate a proteid-free transudate from a fluid such as blood-serum, a certain amount of work had to be done, and that for this separation a minimum difference of pressure on the two sides of the filtering membrane of at least 28 mm. Hg was necessary. The intra-ocular fluid has such a small content in proteid that it may be regarded as analogous in all respects to the fluid which is supposed to be separated by the glomeruli of the kidney. In order, therefore, that any fluid shall be poured out in the eyeball a minimum difference of 30 mm. Hg must be present between intra-ocular pressure and capillary blood-pressure. If this pressure difference is not present, work must be done by the

cells forming the filtering membrane, and the formation of intra-ocular fluid must be regarded in the light of a secretion rather than in that of a transudation. A definite decision on this point could be reached if there were any means of determining the blood-pressure in the capillaries of the eyeball. Niesnamoff's arguments involve several fallacies. In his experiments he connected a cannula, attached to a reservoir of salt solution, with the eyeball of a living animal. He found that the fluid neither ran in nor out at 25 mm. Hg, which was therefore the intra-ocular pressure. He then determined the rate of inflow when the pressure in his cannula was raised to 50 mm., 75 mm., and 100 mm. Hg. He then killed the animal, and again determined the rate at which the fluid would flow in under these various pressures. He found that above 50 mm. Hg, the rate of inflow was the same in the dead as in the living animal. He therefore concluded that 50 mm. Hg represented the intra-capillary pressure. In coming to this conclusion he was guided by the assumption that, when the intra-ocular pressure was raised so as to be equal to the intra-capillary pressure, the transudation of intra-ocular fluid would cease and above this pressure the rate of inflow for his reservoir would be, therefore, the same in the living and dead eye. It is impossible, however, by this method to determine intra-capillary pressure. The globe of the eyeball is practically rigid. As the intra-ocular pressure is raised the intra-ocular fluid will press upon the veins of the ciliary processes, and the blood-pressure will therefore rise in the capillaries and in the veins until it is greater than the intra-ocular pressure. With successive rises in the intra-ocular pressure the pressure in capillaries and veins must get larger and larger in order that any circulation of blood may be maintained, and the circulation through the capillaries will cease only when the intra-ocular pressure is very nearly as high as the arterial pressure. If the circulation in Niesnamoff's experiments ceased at 50 mm. Hg, it is evident that the normal intra-capillary pressure, when the intra-ocular pressure is 25 mm. Hg, must be considerably below 50 mm. Hg. How, then, are the very definite figures obtained by Niesnamoff to be explained? This observer apparently performed very few experiments. In his paper he gives the results of only one such experiment as that here described. On repeating his experiments Henderson and Starling found it impossible to obtain anything like such definite figures—and this for various reasons. In the first place, a considerable rise of intra-ocular pressure such as to 50 or 70 mm. Hg, exercises an abnormal stretching effect upon the filtering apparatus of the eyeball, so that the channels at the anterior angle of the eye are gradually opened up, and in many experiments a consequent gradual increase in the rate of inflow of the fluid was observed. In most experiments, for example, the rate of inflow was greater with descending pressures than with ascending pressures. This is well shown in experiment No. 2, on p. 972.

The following experiment shows the dilatation consequent on a preliminary raising of the intra-ocular pressure :

Cat, anæsthetised with Ether. Eserin applied locally to Conjunctival Sac. Pupil moderately contracted.

B.P. in mm. Hg.	I.O.P. in mm. Hg.	Rate of absorption in cubic millimetres per minute.
110	16	0
110	32	5
110	48	8
108	64	9
112	16	0
112	32	8
112	48	13
112	64	18

Another disturbing factor is the size of the pupil (*v. infra*). Unless atropin be given at the beginning of the experiment, the observations on the living eye are made with a somewhat contracted pupil, whereas those on the dead eye are made on a widely dilated pupil. Other factors being equal, the filtration in the eye with dilated pupil is always slower than in the eye with contracted pupil. In certain of their experiments Henderson and Starling observed an equality of inflow between the dead and living eye at some pressure above 40 mm. of mercury, but on further raising the pressure this equality disappeared, showing that they were dealing with yielding tissues and altering membranes. This fact rendered it impossible to obtain by such methods any definite information of the intra-capillary pressure in the eyeball, or of the level or intra-ocular pressure at which transudation or formation of intra-ocular fluid would definitely cease. One other factor which would aid in disturbing the results obtained is the effect of a high intra-ocular pressure on the general circulation through the eye-ball. If the pressure is raised to such a height that the circulation is entirely abolished, changes must rapidly take place in the apparatus both for formation and absorption of intra-ocular fluid, and subsequent results cannot be compared with those obtained before such a cessation of circulation. The raising of the intra-ocular pressure in itself may act as a stimulus and cause reflexly alterations in blood-flow, in the general blood-pressure, or in the state of contraction of the pupil. The co-operation of these various factors suffices to explain the varying results obtained in the very many experiments performed upon this subject, including those of which details have already been given. Henderson and Starling conclude, therefore, that the results obtained by Niesnamoff must be regarded as accidental, and that a greater number of experiments would have convinced this observer of the fallacies of his method.

Although it is impossible at present to determine the intra-capillary pressure in the ciliary processes, we may at any rate inquire whether there is, in all experiments on the subject, the possibility of a difference of pressure of 30 mm. Hg between intra-capillary blood-pressure and intra-ocular pressure. In the case of a similar question in the kidney, we have been accustomed to compare the aortic blood-pressure with

the ureter pressure, and have regarded a difference of 40 mm. between these two pressures as satisfying the necessary conditions for filtration through the glomeruli. A similar comparison of arterial blood-pressure and intra-ocular pressure leads to the same result. Henderson and Starling give the intra-ocular pressure and arterial pressure as determined in a series of 20 experiments. It will be seen that in every case there is a difference between the two pressures of at least 48 mm. Hg, the average difference of pressure in all the experiments being 84·8 mm. Hg.

Animal.	B.P. in mm. Hg.	I.G.P. in mm. Hg.	B.P.—I.O.P.
Cat . . .	130	16	114
Cat . . .	140	25	115
Cat . . .	138	20	118
Cat . . .	94	24	70
Rabbit . .	74	16	58
Dog . . .	112	14	98
Cat . . .	104	15	89
Cat . . .	106	19	87
Cat . . .	106	18	88
Cat . . .	120	20	100
Cat . . .	150	22	128
Dog . . .	84	12	72
Dog . . .	58	10	48
Dog . . .	70	16	54
Cat . . .	115	23	92
Cat . . .	124	32	92
Cat . . .	110	16	94
Cat . . .	138	22	116
Cat . . .	94	27	67
Cat . . .	110	24	96

The observations of Henderson and Starling, therefore, tend to support in every particular the view laid down by Leber, namely that intra-ocular fluid is produced in the ciliary processes by a process of filtration, and that the sole factor determining the amount of transuded fluid is the difference of pressure between the blood in the capillaries and the fluid in the eye-ball.

Hovius.—De circulari humorum motu in oc., 1702. Adamük.—Sitzungsberichte d. Wiener Akad., lix, 1869. Jesner.—Pflüger's Archiv, xxiii, 1880. Priestley Smith.— Ophth. Rev., vii, 1888; Glaucoma, London, 1891. Bentzen and Leber.—A. f. O., xli, 3, 1895. Niesnamoff.—A. f. O., xlii, 4, 1896. Bellarminoff.—A. f. O., xxxix, 3, 1893. Leber.— Internat. Congress, Utrecht, 1899. Ehrlich. — Deutsche med. Woch., 1882. Greeff.—A. f. A., xxviii, 1894. Bauer.—A. f. O., xlii, 1, 1896. Leplat.—Ann. d'Oc., ci, 1889. Starling.—Jl. of Phys., xix, 1896. *Henderson and Starling.—Proc. Roy. Soc., B, lxxvii, 1906. *Leber.—In G.-S., 1903.

The intra-ocular lymph is secreted entirely, or almost entirely, by the ciliary processes. In lower animals, e. g. the rabbit, in which the ciliary processes extend forwards on to the back of the iris this structure takes some part in the secretion, but in man little or none of the aqueous is derived from the back of the iris. That the ciliary processes are well adapted to secretory functions is shown by their anatomical peculiarities, especially in their very rich vascular supply and

in the folds and depressions which so enormously increase their super-ficial area.   That the iris has little to do with the secretion of lymph is shown by the cases of congenital aniridia, in which there is no lack of aqueous but even a tendency to glaucoma (q. v.).

The results of a complete ring synechia show that the fluid is secreted behind the iris, as was pointed out by Méry and Beer.   As the lymph is then imprisoned behind the iris and prevented from pass-ing into the anterior chamber and so out by the filtration angle, the iris becomes bulged forwards like a sail and the so-called iris bombé results. It is not surprising that under these circumstances the anterior chamber still contains aqueous, for the bowing forwards of the iris causes blocking of the angle, and thus prevents its escape ; moreover the ring synechia is not always complete in these cases, but only so far advanced that the communication between the posterior and anterior chambers is inadequate.

The formation of anterior staphyloma as the result of perforation of the cornea, prolapse of the iris, and adhesion of the pupillary margin to the edges of the aperture confirms the origin of the lymph from the ciliary body.   The perforation leads to intense hyperæmia of the iris, as is best seen in the albino rabbit.   In spite of this hyperæmia, which would tend to increase any secretion from the anterior surface of the iris, the anterior chamber becomes completely abolished and the whole surface of the iris is pushed forwards and stretched out over the back of the cornea.   The fluid then accumulates in the posterior chamber, which becomes much enlarged.

The absence of secretion from the anterior surface of the iris can be demonstrated experimentally in the rabbit.   A rod with a small circular metal plate at the end is passed through the pupil, so that the plate lies behind the iris.   The iris is then caused to contract strongly around the rod by means of eserin ; this prevents fluid from passing through the pupil.   Owing to the diminished intra-ocular pressure the conditions are then more than usually favourable for secretion, but in spite of this fact no fluid appears upon the surface of the iris, as shown by testing with blotting-paper.   The objection that secretion is abolished by the action of air and lowering of temperature (Ham-burger) is insufficient to account for the phenomenon (Leber).   By a modification of the method the iris is clamped between two metal plates, and the rod is replaced by a tube which is connected with a manometer. In favourable experiments a rise of several mm. Hg is obtained in the manometer, thus proving the secretion of fluid behind the iris.   The experiments are difficult owing to the extensibility of the iris tissue (Leber).

The most conclusive proof that the lymph is secreted by the ciliary processes is found in the results of removing them from the eye.   It is possible in the rabbit to remove the whole of the iris and ciliary pro-cesses through a corneal section (Leber, Deutschmann).   It is found that no fluid is then secreted, and that which exists in the vitreous becomes absorbed, so that the eye shrinks and is almost entirely filled by the lens.   Since removal of the iris alone in man causes no marked diminution in the intra-ocular pressure this must be due to the removal

of the ciliary processes. The iris cannot be completely ablated in the rabbit without the ciliary processes, though this is possible in the dog (Nicati).

Evidence as to the site and method of secretion of lymph in the eye may also be derived from the subcutaneous or intravenous injection of chemical substances which can be recognised by their colour (e. g. fluorescein) or by special tests (e. g. potassium ferrocyanide, potassium iodide, etc.). These experiments will be recorded later, but it may be stated here that Ehrlich concluded from his fluorescein experiments that the aqueous is secreted from the anterior surface of the iris ; this view is supported by Hamburger. Evidence will be given later which proves beyond dispute that absorption readily occurs at the anterior surface of the iris. It is à priori improbable that the same mechanism should subserve diametrically opposite functions.

The choroid has been held by many to take part in the secretion of aqueous. Anatomical considerations render it improbable that fluid secreted by the choroid passes either inwards into the vitreous, in which case it would have to percolate through the retina, or forwards into the posterior chamber. The latter view has been adopted by Nicati, who considers that the fluid passes along beneath the membrana vitrea, but of this there is no evidence. It is known that the choriocapillaris supplies nutriment to the outer layers of the retina, and it is unlikely that any considerable excess of lymph beyond that required for this purpose is secreted. This does not necessarily eliminate the possibility of abnormal secretion and transudation through the retina, etc., in pathological circumstances (v. Vol. II, p. 432). The strongest evidence against secretion of aqueous by the choroid is found in the results of ablation of the iris and ciliary processes in the rabbit.

The same arguments apply à fortiori to the retina, the blood-vessels of which solely subserve the nutrition of the membrane itself. That the vitreous takes any active part in secretion is improbable, or even impossible, though it has been conjectured by several authorities. It possesses no vascular system, and the results of the injection of test solutions all favour a ciliary origin for the fluid ; moreover, they demonstrate the excessively slow metabolism of the vitreous, fluorescein, for example, remaining as long as two or three weeks in the vitreous before it disappears by a process of slow diffusion.

MÉRY.—Mém. de l'Acad. des Sc., 1707. BEER.—Ansicht d. staph. Metamorph. d. Auges, Wien, 1806. HAMBURGER.—K. M. f. A., xxxviii, 1900. LEBER.—Internat. Congress, Utrecht, 1899. DEUTSCHMANN.—A. f. O., xxvi, 3, 1880. NICATI.—A. d'O., x, 1890 ; xi, 1891. EHRLICH.—Deutsche med. Woch., 1882.

The conditions which obtain in the fœtal eye are of some interest and importance in this connection. Early observers denied the existence of an anterior chamber at birth (Petit), though they admitted the presence of fluid in the posterior chamber (Haller) ; others assumed the possibility of secretion from the anterior surface of the iris (Zinn) ; v. Kölliker proved the early development of the anterior chamber, and it is undoubtedly well formed, though shallow, during the lengthy period in which the pupillary membrane is intact. It is improbable

that the rudimentary iris secretes the aqueous, as held by Hamburger. The pupillary membrane is essentially a capillary network, specially adapted to secreting fluid for the nourishment of the growing lens; it is most likely that it also provides the lymph for the small anterior chamber. The possibility that it is permeable to fluid secreted by the ciliary processes must not be overlooked, though it is unlikely. The fact that the pressure in the vitreous chamber and in the anterior chamber is the same in the adult eye does not prove that identical conditions obtain in the fœtal eye, so that filtration through the pupillary membrane cannot be excluded. In any case it would not be justifiable to reason from the fœtal eye to the adult, and our knowledge of the physiology of the former is too defective for much stress to be laid upon it. It is probable that the vessels in the vitreous play an important part in secretion in the eye before birth (*cf.* p. 847).

Lower animals which do not possess ciliary processes are usually provided with some mechanism which is similar anatomically, and probably also physiologically, such as a pecten or a vascular system in the vitreous (Leuckart).

Petit.—Mém. de l'Acad. des Sc., 1728. Haller.—Elem. Physiologie, v, 1757. Zinn.—Descr. anat. oc. hum., 1780. Hamburger.—B. d. o. G., 1902. Leuckart.—In G.-S., ii, 1876.

If the evidence in favour of the secretory function of the ciliary processes be considered conclusive, there still remains the question of the exact mechanism of secretion. We have hitherto used the term "secretion" in a general sense, prejudicing no special theory. In general physiology it is perhaps advisable to restrict the term to those cases in which fluid is produced, or can be produced, under conditions which are apparently contrary to ordinary physical laws. Thus, in the salivary glands saliva may be secreted against a pressure which far exceeds the blood-pressure in the carotid artery. It is obvious that this phenomenon cannot be explained upon the ordinary physical laws of filtration, though an increased knowledge of osmotic pressures may still reconcile it with physical processes of a different nature. Early observers, *e. g.* Mérv (1707), regarded the ciliary body as a whole as a gland, specially differentiated for the secretion of aqueous. More recently an attempt has been made to narrow down the glandular elements of the ciliary body to the epithelium (Boucheron, Nicati, Treacher Collins). The last-mentioned author regards the tubular outgrowths of epithelium in the pars plana as specific glands, specially concerned in the secretion of aqueous (*v.* Vol. I, p. 335).

The arguments against considering the ciliary body, or any part of it, as a gland, subserving secretion in the narrower sense of the term, have already been indicated. On the anatomical side the ciliary body as a whole in no way resembles a true gland, and the tubular depressions of the pars plana bear only a superficial similarity to true tubular glands elsewhere. On the other hand, the anatomical arrangements are exactly suited to the transudation of fluid by filtration, as is shown by the increase of superficial area by folding and reduplication, the extreme vascularity, etc. On the physiological side there is no proof

of any true secretion; *i.e.* no experiment has yet been devised proving the possibility of secretion of fluid by the ciliary body against a pressure greater than that of the local intra-vascular pressure. On the other hand, all the experimental evidence is consistent with a transudation of fluid by a simple process of filtration. The production of lymph in the eye therefore follows the laws of lymph-production in other parts of the body, where recent researches have tended to modify the conclusions of Heidenhain, which involved the assumption of a definite vital secretory process (*cf.* Starling).

Whilst these views are the only ones which are justified on the present available experimental evidence, it must yet be remembered that the methods of experiment are comparatively crude when the delicacy and complexity of the anatomical structures and physiological processes are taken into consideration. It is not probable that the epithelium acts as a wholly inert membrane. Slight though the metabolic processes going on in the cells may be, it is probable that they may have far-reaching effects, and evidence is not altogether wanting that such is the case; it is to be found *par excellence* in the results of various immunisation experiments (*v. infra*).

That changes of an important nature occur in the epithelium under abnormal conditions of transudation is proved by Greeff's interesting observations. If the ciliary processes are examined after puncture of the anterior chamber and rapid evacuation of the aqueous, the epithelium shows small cystic formations, which are filled with albuminous and fibrinous exudates, and sometimes red corpuscles and leucocytes. Greeff attributed the albuminous constituency of the aqueous after paracentesis to this raising and desquamation of epithelium. Bauer, however, has shown that there is no parallelism between the times of onset and disappearance of the cysts and the change in the aqueous. The aqueous coagulates ten minutes after puncture, at which time the cystic formation is slight, not becoming maximal until about half an hour after puncture. The coagulability is lost four hours later, whilst the cysts gradually disappear only on the next day, and are still present to a slight extent after six days. Moreover, the fibrin disappears earlier than the proteids, spontaneous coagulation being absent after four hours, whilst after three and a half hours the proteid content is still very considerable. These differences are readily explicable on the theory that the alteration in the aqueous is due to the hyperæmia following lowered pressure, but cannot be explained by the destruction of the epithelium.

Hamburger considered that, the osmotic pressure of the aqueous being higher than that of blood-plasma, the former could not be a simple filtrate from the latter. The determinations of the osmotic pressures were confirmed by Kunst and by Manca and Deganello. The difference is too slight, however, to draw such a sweeping conclusion. Owing to the slowness of its production, the aqueous may undergo concentration in the anterior chamber by backward diffusion of water into the non-secreting anterior iridic vessels, by taking up solids from the tissues, and by drying from the surface of the cornea (Leber).

MÉRY.—Mém. de l'Acad. des Sc., 1707. BOUCHERON.—Soc. d'O., 1883. NICATI.—A. d'O., x, 1890; xi, 1891. TREACHER COLLINS.—T. O. S., xi, 1891. HEIDENHAIN.—Pflüger's Archiv, xlix, 1891; lvi, 1894. STARLING.—Jl. of Physiology, xvi, xvii, 1894, etc. GREEFF.—B. d. o. G., 1893; A. f. A., xxviii, 1894. BAUER.—A. f. O., xlii, 3, 1896. HAMBURGER.—Virchow's Archiv, cxl, 1895. KUNST.—Dissertation, Freiburg, 1895. MANCA AND DEGANELLO.—Ann. di Ott., xxvii, 1898.

Information as to the mode of secretion of the intra-ocular lymph may be obtained from the injection of recognisable foreign substances into the blood-stream. Memorsky investigated the time taken for potassium ferrocyanide to appear in the eye after intravenous injection. In adult dogs it appeared in the aqueous after injection of 0·5 gm. in 18—20 minutes, in the vitreous after 1½ hours. It could not be recovered after subcutaneous injection in the dog, but readily in the rabbit; it was found after injection into the peritoneal cavity, but not after feeding experiments. The effects of subcutaneous injection were confirmed in the rabbit by Ulrich and A. Weber.

Potassium iodide passes very quickly into the eye—in the rabbit in ten minutes after administration of 0·5 gm. by the mouth (Leber); in six to eight minutes with a dose of 0·25 gm. (Schläfke); in three minutes after subcutaneous injection, in six minutes after instillation into the conjunctival sac (Hilbert). After subcutaneous injection of iodoform in man iodine appeared in the anterior chamber in fifteen minutes (Hilbert). Leplat found in the rabbit that potassium iodide appeared in the aqueous in ten minutes, in the vitreous in fifteen minutes, after subcutaneous injection; the quantity in the aqueous and anterior part of the vitreous increased for seven hours, gradually disappearing from this part, and being found finally only in the posterior part of the vitreous, a result which might be expected if the lymph is secreted by the ciliary processes. Confirmatory experiments have been published by Ottolenghi. Vinci found that after subcutaneous injection in the temporal region of the dog potassium iodide or sodium salicylate appeared three to five minutes earlier in the eye of the same side than in the other.

Traces of mercury can be demonstrated by an electrolytic method in the aqueous, after subcutaneous injections of large doses (8 gm.) of calomel (Rampoldi), whilst no trace is found after subconjunctival injection of soluble mercury salts (v. infra).

All these reagents require special chemical reactions for their identification. This objection is removed by using fluorescein, easily recognised by its green fluorescence, which is visible against a dark background in solutions of 1 : 2,000,000. The method was first used by Ehrlich, but the conclusions he arrived at are inaccurate. Watery solutions of potassium fluorescein or uranin (ammonium fluorescein) are used, in rabbits 2—8 c.c. of a 20 per cent. solution for subcutaneous injection, 0·3—1 c.c. of a 5 per cent. solution for injection into the vein of the ear. The results are quite different with the intact eye and after evacuation of the anterior chamber. In the former case the colour appears very rapidly—one minute by intravenous, four minutes by subcutaneous, injection—as a green streak, the so-called Ehrlich's line, passing vertically from the upper part of the iris over the pupil. The line is always vertical, irrespective of the position

of the eye, though the length, breadth, and clearness vary under different circumstances. No passage of green fluid through the pupil can be seen. Ehrlich concluded that the aqueous was secreted from the anterior surface of the iris. This is not true: the line is due to diffusion, and can be readily reproduced by diffusing fluorescein solution against water through an inert membrane, *e.g.* Descemet's, in a U tube (Leber). Moreover, if the aqueous is first evacuated the anterior chamber is seen to fill up by green fluid passing forwards through the pupil. Ehrlich's line is obtained after death on injection of uranin solution into the carotid (Ehrenthal); this can only be due to diffusion, since there is then no difference of pressure between the contents of the vessels and their surroundings.

In the rabbit, after removal of the iris and ciliary processes, the green coloration is not obtained; in the dog, after removal of the iris, the ciliary processes remaining intact, the green colour appears more slowly than in the normal animal (Nicati). This is due to the absence of diffusion and the slowness of true transudation from the ciliary processes.

By increasing the amount of coloured fluid secreted the passage through the pupil may be seen in the intact eye. It is necessary to produce hyperæmia of the ciliary processes or to artificially hasten the secretion of aqueous, as may be done by temporary luxation of the eyeball (Nicati, Hamburger), by section of the sympathetic or trigeminal nerve (Schöler and Uhthoff, Nicati), or by cauterisation of the limbus with silver nitrate, or even simple instillation of eserin or pilocarpin (Wessely).

Hamburger attempts to support Ehrlich's view; he has found that if very small quantities of fluorescein are injected into the posterior chamber a quarter of an hour or more elapses before it comes through the pupil into the anterior chamber. If all the fluid is secreted by the ciliary processes and the whole contents of the anterior chamber are secreted in about three quarters of an hour (*v.* p. 966), one would expect a more rapid transit. Probably the obstacle is to be found in the pressure of the sphincter iridis against the lens (Ulrich), for if the iris is removed the fluid passes forwards continuously (Hamburger).

With subcutaneous injection the coloration of the aqueous is most intense after three to four hours, and gradually diminishes from six to twenty-four hours (Schöler and Uhthoff). With stronger doses examination of the ciliary processes shows that they rapidly become stained, so that after two to three hours the whole ciliary body and back of the iris are deep green, and the anterior part of the vitreous is also coloured. After the fourth hour the coloration of the ciliary body and vitreous quickly diminishes. Ovio confirms with fluorescein the results obtained by Leplat with potassium iodide.

The passage of alexins or anti-bodies into the aqueous is of great interest, but comparatively little work has as yet been carried out upon this subject. Apparently some kinds are absent from the aqueous when present in large quantity in the blood-serum, whilst others, especially if required locally, are present. Nuttall and Buchner consider that normal

aqueous possesses some bactericidal properties. Marthen and Bach found this to be extremely slight for staphylococci and other common bacteria of the conjunctival sac.

Wessely has found that agglutinins and hæmolysins are absent from the normal aqueous after immunisation, but that they appear after irritation, especially after subconjunctival injections of salt solution. The same applies to precipitins, even in the aqueous formed after paracentesis (v. Dungern), though under these circumstances hæmolysins pass into the aqueous (Römer) (*see* Chapter XIX). Römer found agglutinins in the aqueous and in the cornea of rabbits immunised against typhoid bacilli.

Absorption readily takes place from the surface of the cornea and from the conjunctival sac. This subject will be considered when dealing with the nutrition of the cornea.

MEMORSKY.—A. f. O., xi, 2, 1865. ULRICH.—A. f. O., xxvi, 2, 1880. AD. WEBER.—Internat. Med. Congress, London, 1881. SCHLÄFKE.—A. f. O., xxv, 2, 1879. HILBERT.—In Nagel's Jahresbericht, 1884. LEPLAT.—Ann. d'Oc., xcviii, 1887. OTTOLENGHI.—Ann. di Ott., xv, 1886. VINCI.—Ann. di Ott., xxx, 1901. RAMPOLDI.—Ann. di Ott., xvii, 1888. EHRLICH.—Deutsche med. Woch., 1882. EHRENTHAL.—Dissertation, Königsberg, 1887. NICATI.—A. d'O., x, 1890; xi, 1891. SCHÖLER AND UHTHOFF.—Jahresbericht ü. d. Wirksamkeit d. Augenklinik, 1881. WESSELY.—A. f. O., l, 1900. HAMBURGER.—C. f. A., xxii, 1898; K. M. f. A., xxxvii, 1899; Deutsche med. Woch., 1899; K. M. f. A., xxxviii, 1900; xxxix, 1901; B. d. o. G., 1902. ULRICH.—B. d. o. G., 1896. OVIO.—XI Internat. Med. Congress, vi, 1895. NUTTALL.—Z. f. Hyg., iv, 1888. BUCHNER.—Arch. f. Hyg., x, 1890. MARTHEN.—B. z. A., xii, 1893. BACH.—A. f. O., xl, 3, 1894. WESSELY.—K. M. f. A., xl, 1902; Deutsche med. Woch., 1903. v. DUNGERN.—Die Antikörper, Jena, 1903. RÖMER.—A. f. O., liv, 1, 1902; lvi, 3, 1903.

Numerous experiments have been directed to deciding the action of nerves upon the secretion of the intra-ocular lymph. The one point which is put almost beyond dispute is that there are no special secretory nerves. Stimulation and section of various nerves have a considerable influence upon the secretion, but it is entirely in an indirect manner through their action upon the blood-vessels. These effects will be dealt with in treating of the intra-ocular pressure; only special experiments upon the actual production of lymph will be enumerated here.

Schöler and Uhthoff found that the passage of fluorescein through the pupil into the anterior chamber was hastened by section of the cervical sympathetic or extirpation of the superior cervical ganglion. Nicati found it unaltered on the same side, whilst it was slowed on the opposite side, an effect which he attributed to lowering of the general blood-pressure. Hemisection of the cervical cord causes slowing on each side, most marked on the opposite side. Langendorff finds a difference between the effect of section of the cervical sympathetic and that of extirpation of the superior cervical ganglion. Six days after the operation Ehrlich's line appeared much later on the ganglion side than on the other; this is attributed to hyperæmia persisting after section of the nerve, whilst it is followed by constriction when the ganglion is extirpated. Wessely found that the anterior chamber refilled more slowly after puncture when the sympathetic was stimulated by faradisation; moreover the aqueous did not coagulate, and it contained only 0·04 per cent. of proteids. Lodato found some days after

extirpation of the superior cervical ganglion increase in the refractive index of the aqueous, due to increase in proteids (four or five times the normal), the sodium chloride and alkalinity remaining constant.

After section of the trigeminal Grünhagen and Jesner found increase of proteids and fibrin on the same side and to a less extent on the opposite side; this was confirmed by Nicati and Ollendorff. The same effect is seen after hemisection of the medulla oblongata (Grünhagen and Jesner). Schöler and Uhthoff obtained the same effect with fluorescein after section of the trigeminal as after section of the sympathetic. The experiments were confirmed and modified by Nicati. It must be remembered that section of the trigeminal anterior to the Gasserian ganglion includes also the sympathetic fibres. Nicati found the effect diminished on section proximal to the ganglion, but this was probably owing to lowered blood-pressure, the result of opening the skull.

Most of these experiments are of very little importance. In scarcely any of them was the blood-pressure registered simultaneously, and such experiments are worthless. The subject would repay further investigation with more accurate control of the conditions.

SCHÖLER AND UHTHOFF.—Jahresbericht ü. d. Wirksamkeit d. Augenklinik f. 1881. NICATI.—A. d'O., x, 1890; xi, 1891. LANGENDORFF.—K. M. f. A., xxxviii, 1900. WESSELY. —B. d. o. G., 1900. LODATO.—Arch. di Ott., ix, 1901. GRÜNHAGEN AND JESNER.—C. f. A., iv, 1880. JESNER.—Pflüger's Archiv, xxiii, 1880. OLLENDORFF.—A. f. O., xlix, 1900.

The effect of irritation of the eye upon the constitution of the aqueous has been investigated. Adamük found that chemical irritation of the conjunctiva caused increased flow after puncture of the cornea. Jesner found increased proteid and fibrin after cauterisation of the limbus; this was confirmed by Bach, who also obtained the same result after prolonged painting of the cornea with 1 in 1000 perchloride of mercury, etc. Wessely obtained little result from mechanical irritation, more from faradisation, and most from chemical irritation, especially when this extended to the iris, etc. Subconjunctival injection of 5 per cent. salt solution causes a considerable increase in proteids and the formation of fibrin; hæmolysins and agglutinins are also increased in immunised animals (Wessely). An effect upon the other eye has been observed by some authors (Grünhagen and Jesner, Bach, and others); this question will be considered when dealing with sympathetic ophthalmia.

Wessely has investigated the effect of subconjunctival injection of suprarenin upon the amount and nature of the aqueous. If fluorescein is injected into the vein of the ear of a rabbit a quarter of an hour after subconjunctival injection of suprarenin no Ehrlich's line appears on the same side though it is present on the other. If the anterior chamber is then punctured it refills very slowly, and the tension remains subnormal. The aqueous does not coagulate spontaneously, and contains little more (0·05 per cent.) than the normal amount of proteid. The effect lasts only about one and a half to two hours, i. e. the time required for absorption, the suprarenin being rapidly excreted from the body. If no paracentesis is performed the tension rises later, reaching with $\frac{1}{2}$ per cent. solution its maximum in three and a half hours, falling to the

normal in six hours. Addition of suprarenin to subconjunctival saline solutions prevents the increase of proteid and formation of fibrin in the aqueous, as well as the formation of Greeff's cysts in the ciliary processes.

Strong cocain solutions slow the re-formation of the anterior chamber after paracentesis according to Panas, but Nicati could observe no such effect.

After eserin the aqueous becomes more quickly coloured on sub-cutaneous injection of fluorescein (Ulrich), and this disappears more rapidly than usual (Schöler and Uhthoff, Ulrich, Wessely) ; the same occurs with pilocarpin (Wessely). The effect is due to the dilatation of the iris vessels (Ulrich) and to the increased surface of the con-stricted iris, both factors tending to promote diffusion. The effect of eserin has been exhaustively investigated by Grönholm, by Leber and Niesnamoff's method. He concludes that the rate of secretion is reduced by a half, and the amount of the blood in the eye is greatly reduced.

Adamük found that atropin caused diminished secretion, attributed to vaso-constriction ; this observation requires further investigation.

With curare and artificial respiration Jesner found increase of proteids and spontaneous coagulation.

Henderson and Starling have recently made experiments to decide the effect of the size of the pupil on the absorption of intra-ocular fluid. One eye of the animal under observation was treated with eserin and the other with atropin. The instillation of these drugs should be begun before the induction of anæsthesia, as the action of eserin is very uncertain if only instilled after anæsthesia.

They found, as a result of these experiments, that the intra-ocular pressure in the two eyes remains the same during the time of observation, but that, if the pressure in the apparatus be raised, the rate of filtration in the eye under eserin is much greater than in that under atropin.

It is difficult to give a precise explanation as to the cause of this difference. Stretching of the filtration spaces at the angle of the anterior chamber may possibly account for it all. If this, however, is the case, we should expect to find the intra-ocular pressure at a lower level in the eye with the contracted pupil, for the intra-ocular pressure must, of course, be the product of the rate of secretion and the rate of absorption of the intra-ocular fluid. The same objection applies to the explanation of this phenomenon by Grönholm, who states that, in his opinion, it is due to diminished intra-ocular secretion as a result of the contraction of the intra-ocular vessels. It may also be possible that at these raised pressures other channels of filtration are opened up—such, for instance, as the surface of the iris. An important, perhaps the most important, factor, however, must be the crushing of the dilated flaccid iris into the filtration angle of the eye, thus causing a mechanical obstruction, which will be more marked the greater the intra-ocular pressure. Hence the smaller amount of filtration in the atropinised or dead eye with dilated pupil, as compared with that in the eye which has been put under the influence of eserin.

The figures of a typical experiment are given.

Cat, anæsthetised with Ether. Blood-Pressure Average 138 mm. Hg, with only trifling Variations throughout the Experiment.

Intra-ocular pressure in mm. Hg.	Rate of filtration in eserin eye in cubic millimetres per minute.	Rate of filtration in atropin eye in cubic millimetres per minute.	Rate of filtration in atropin eye *post mortem*, in cubic millimetres per minute.
20	0	0	15
35	11	8	20
50	16	11	25
65	23	14	31

ADAMÜK.—Sitz. d. Wiener Akad., lix, 1869. JESNER.—Pflüger's Archiv, xxiii, 1880. BACH.—A. f. O., xlii, 1, 1896. WESSELY.—A. f. O., l, 1900; K. M. f. A., xl, 1902; Deutsche med. Woch., 1903; B. d. o. G., 1900. PANAS.—A. d'O., vii, 1887. NICATI.—A. d'O., x, 1890; xi, 1891. ULRICH.—A. f A., xii, 1883. GRÖNHOLM.—A. f. O., xlix, 1900. HENDERSON AND STARLING.—Proc. Roy. Soc., B. lxxvii, 1906.

Lymph=excretion.—The lymph which is secreted by the ciliary processes passes for the most part forwards from the posterior chamber through the pupil into the anterior chamber. None traverses the iris, as has been held by Ulrich and others. That the pressure of the iris on the lens produces some hindrance—a physiological seclusion of the pupil—to the passage of fluid must be admitted with Ulrich and Hamburger; it is, however, of slight moment. Ulrich based his views on experiments in which he injected potassium ferrocyanide into the vitreous; after enucleating and testing with ferric chloride, the ciliary margin of the iris was found to be deeply stained. There can be little doubt that this is due to diffusion, most marked here owing to the proximity of the ciliary processes (Leber). Koster has shown that the iris is impermeable to fluid by filtration under pressures of 5—10 mm. Hg kept up for many hours, or of 20 mm. Hg for at least a quarter of an hour. This is due, not to the resistance of the stroma, but of the retinal epithelium and smooth muscle. Leber has repeated Hamburger's experiment of injecting small quantities of reagent into the vitreous near the ciliary processes. With Chinese ink, in which case there is no question of diffusion, the particles appear in the pupil in eleven to thirteen minutes. Nuel and Benoît found that in man particles of ink appeared in the pupil after injection of one to two drops into the vitreous, an amount which could have no appreciable effect upon the pressure in the vitreous chamber. It may, therefore, be considered proved that under normal conditions all the fluid passing forwards from the ciliary body goes through the pupil.

ULRICH.—A. f. O., xxvi, 3, 1880; A. f. A., xx, 1889; B. d. o. G., 1896. HAMBURGER.—C. f. A., xxii, 1898; Deutsche med. Woch., 1899. KOSTER.—A. f. O., xli, 2, 1895; A. f. A., xxxviii, 1898. NUEL AND BENOÎT.—A. d'O., xx, 1899.

The aqueous passes out of the anterior chamber by three routes : (1) through the spaces of Fontana into the anterior ciliary veins by way of the canal of Schlemm ; (2) through the anterior surface of the iris ; (3)

through the ciliary body, a small part of which, it must be remembered, enters into the boundaries of the chamber.

It was formerly thought that the aqueous passed through the cornea. It was demonstrated by Leber that this was impossible under normal circumstances. He found that the living or fresh cornea is absolutely impervious to fluid by filtration until the pressure reaches 200 mm. Hg—*i. e.* about eight times the normal intra-ocular pressure, and probably four times the intra-capillary pressure. It is, therefore, impossible that fluid should pass through the cornea even under the highest tension found in glaucoma. Leber found that the substantia propria and Descemet's membrane were freely permeable, the former becoming cloudy when œdematous. The protection to the passage of water into the cornea is therefore to be found in the endothelium lining the posterior surface. This is further proved by pathological and experimental (*v. infra*) observations, in which the endothelium is destroyed.

LEBER.—A. f. O., xix, 2, 1873.

The anatomical conditions at the angle of the anterior chamber are admirably adapted to filtration. The blood-vessels are reduced to mere endothelial tubes, and their walls are firmly adherent to the surrounding sclerotic, so that the lumen is kept constantly open. The close relationship of the insertion of the ciliary muscle may assist in this result during life, but experiments on the excised eye show that it is of subsidiary importance. Schwalbe first showed that the anterior ciliary veins were easily injected from the anterior chamber, and concluded that there was a free and open communication. This view was opposed by Leber, and the question was long a subject of dispute. The arguments brought forward by Leber were, however, incontestable, and Schwalbe finally admitted his conclusions. On the anatomical side it was shown that the anterior chamber could not be injected from the blood-vessels, which, on the theory of open communication, could only be explained by a system of valves, and no such valves can be demonstrated. Further, if there was an open communication, it would be impossible to understand how the tension could be kept raised for an indefinite time, or why, on emptying the anterior chamber, it does not immediately become filled with blood.

If a solution of carmin is injected into the anterior chamber of a fresh eye under constant pressure, the episcleral venous network around the cornea after a short interval becomes filled with the coloured fluid, which also runs out of the cut anterior ciliary veins. If there were an open communication between the anterior chamber and the veins the fluid would run out at once; though the interval is short—one or two minutes—it is sufficient to show that some process, such as filtration, is taking place. Moreover, the rapidity of outflow varies with the pressure of injection, and is more rapid the longer the experiment takes place after the death of the eye—*i. e.* the greater the disorganisation of the endothelium of the vessels. Further, if the fluid contains suspended particles, these gradually block the tissue-spaces, impede filtration, and diminish the velocity of outflow. Most important is the apparently

parallel relationship between the pressure and the amount of fluid excreted, a parallelism which can only be explained on the theory of a physical process of filtration.

Very striking are the results of comparative experiments with diffusible and with colloid solutions, such as Berlin blue. The latter substance is precipitated in finely divided form by the saline constituents of the aqueous, and the coloured fluid passes only slightly, or not at all, into the circumcorneal vessels. If a mixture of carmin and Berlin blue is injected, only the red passes through into the vessels. Leber originally thought that Berlin blue did not pass through at all; if, however, the anterior chamber is previously evacuated, it passes through readily, since the dye is not then precipitated. Pagenstecher injected Berlin blue into the human eye in two cases shortly before death; one eye had atropin instilled, the other eserin. In the former no injection of the circumcorneal vessels occurred, whereas it did in the latter, so that constriction of the pupil has a marked effect in improving the conditions of filtration.

Numerous experiments have been performed in which Indian ink has been injected into the eye (Gifford, Gutmann, Leber and Bentzen, Nuel, Asayama, Paterson, and others). The fluid should be examined with the microscope before injection, in order to be certain that the particles of ink are finely divided; they have a tendency to clump together, which is liable to frustrate the experiment. Further, care must be taken not to lose aqueous during injection, as the fresh aqueous secreted may clot and imprison the particles of ink in the meshes of the fibrin network. In satisfactory experiments it is found that Indian ink injected into the anterior chamber passes readily into the circumcorneal vessels. This was at first considered due to stomata between the endothelial cells through which the particles passed. There is no histological evidence that any such stomata are present, but the penetration is seen to take place along the lines of apposition of the cells through the cement substance. The same may occur, though after a much longer interval, after injection into the vitreous (Nuel).

Leber has shown that in the living rabbit indigo carmin in $\frac{3}{4}$ per cent. NaCl solution, injected under low pressure into the anterior chamber, passes readily into the circumcorneal veins.

Henderson and Starling, in a series of animals, determined the intra-ocular pressure under the two conditions (a) with normal intra-ocular fluid, (b) after replacing this fluid by blood serum.

They also compared the relative rates of filtration of normal salt solution and of serum in the living and dead eye.

In their experiments one eye of the animal was connected with a reservoir and manometer containing Ringer's saline fluid, while the other was connected with a similar apparatus filled with filtered blood-serum.

In order to determine the intra-ocular pressure in an eye in which the normal aqueous humour had been replaced by serum, after introduction of the hollow needle, the aqueous was allowed to escape through the side opening in the cannula. Serum was then allowed to flow in for a time, and then the contents of the anterior chamber again

allowed to escape. The side tube was then closed, an air-bubble intro-
duced into the capillary tube, and the pressure determined at which
the bubble moved neither backwards nor forwards.

In nearly every experiment the intra-ocular pressure, during the
first five or ten minutes after the insertion of the cannula, was higher
in the eye filled with serum than in the eye filled with normal fluid.
The difference, however, rapidly diminished, so that fifteen to twenty
minutes after the beginning of the observation the pressures were prac-
tically identical in the two eyes, and remained so throughout the rest
of the experiment. It must be remembered that with the zero method
used there is no movement of fluid into the eye. Hence the fluid
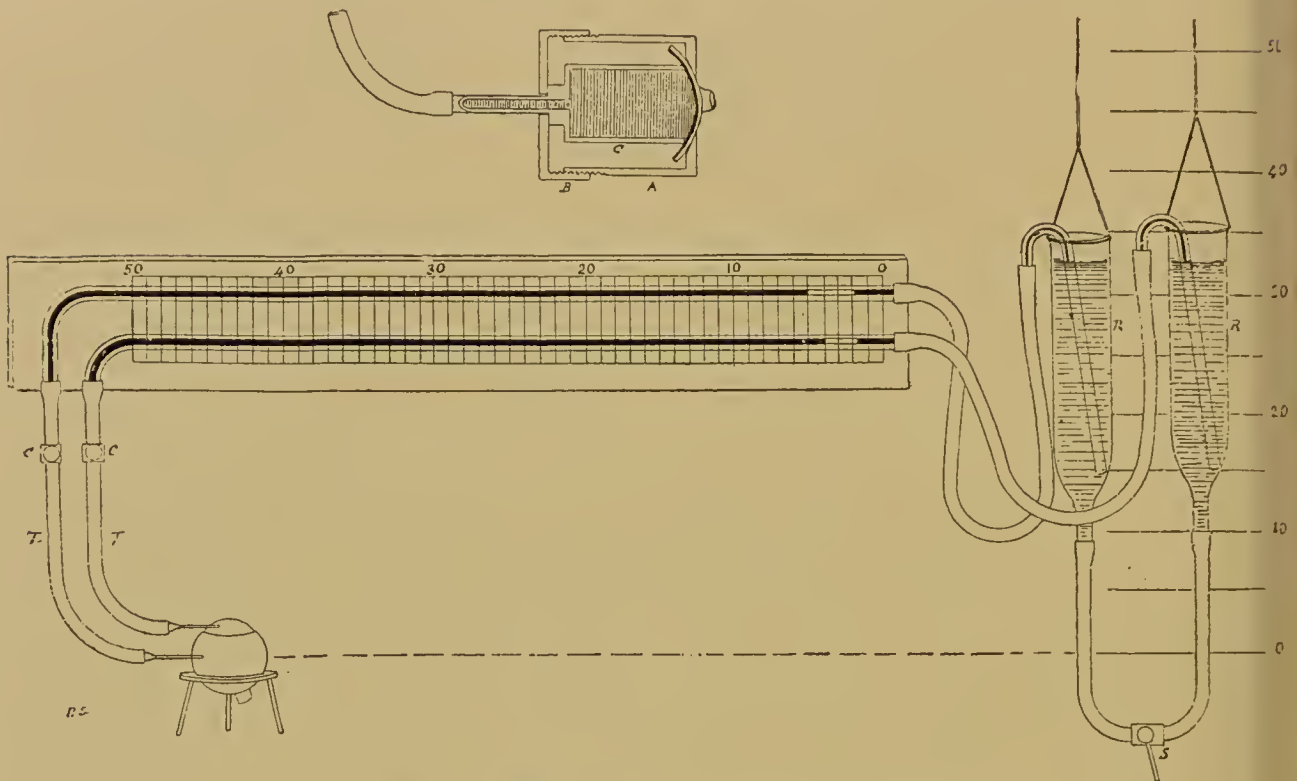
FIG. 689.—PRIESTLEY SMITH'S INJECTION APPARATUS.

Apparatus for injecting fluids under known pressures into the aqueous and
vitreous chambers, and for measuring the amounts of fluid which pass through the
chambers in a given time. The smaller figure shows an apparatus for testing the
escape of fluid through the papilla.

necessary to replace the loss by filtration and to maintain the intra-
ocular pressure is being constantly secreted by the ciliary processes,
and is probably of the normal composition—*i. e.* practically free from
proteid. We should therefore expect a gradual decline of the intra-
ocular pressure in the eye with serum, although hardly so rapid an
equalisation of the pressures on the two sides as was actually observed
in the experiments.

After the determination of the intra-ocular pressure the animal was
killed by opening its heart, and the inflow of serum and saline fluid
respectively observed, first under the normal intra-ocular pressure and
then under raised pressures.

The results of two such experiments are given below. It will be seen that there is a marked difference in the rate of filtration of the two fluids, that of serum being, as one might predict, very much slower than that of saline.

Experiment 1.—Dog, A.C.E., Morphia, Curare, Vagi cut.

Time.	Blood-presure.	Intra-ocular pressure.	
		Salt eye.	Serum eye.
4.15	70 mm. Hg.	26·2	29·4 cm. water.
4.20	70 ,,	24·2	27 ,,
4.45	100 ,,	29·2	29 ,,
Animal killed by opening heart.			

Pressure.	Inflow per minute in cubic millimetres (after 10 minutes).	
	Salt.	Serum.
29 cm.	11·5	6
—	11·5	6
—	11·5	6

Experiment 2.—Cat, Ether, Morphia, Curare.

Time.	Blood-pressure.	Intra-ocular pressure.	
		Salt.	Serum.
3.0	120	14·8	15·1
3.10	116	10·8	12·5
3.20	110	9·2	11·5
Animal killed.			

Inflow three minutes later at same intra-ocular pressures:

Salt.					Serum.
6	.	.	.	.	3
5	.	.	.	.	3·5
5	.	.	.	.	6
5	.	.	.	.	4
4	.	.	.	.	4

Fifteen minutes later:

3·5	.	.	.	.	1·5
3·0	.	.	.	.	1·5
3·5	.	.	.	.	1·5

The difference in the rate of filtration of the two fluids becomes greater the higher the intra-ocular pressure is raised.

The dilution of the blood in the anterior ciliary veins, which must necessarily occur, has been investigated by Lauber. He found in the rabbit that the red corpuscles here numbered 2·9 million as compared with 3·2 million in the vein of the ear, and 3·6 million in a vein of the front paw; there were 2·5 million in the sagittal sinus, where the conditions resemble those in the ciliary veins.

Leber and Priestley Smith showed first that on injection of indifferent fluid into the vitreous of freshly-excised eyes the filtration is much slower. If cannulæ are inserted into both anterior chamber and vitreous, and the pressure in the vitreous is at all higher than that in the anterior chamber, then the lens and iris are driven forwards so that the periphery of the iris comes in contact with the cornea, and the filtration angle is blocked. Filtration is then almost completely abolished (Priestley Smith). This observation, taken in conjunction with the epoch-making discovery of Knies and Ad. Weber of the blocking of the angle in glaucoma by adhesion of the periphery of the iris to the cornea, is of great practical importance. Leber and Bentzen showed that filtration from the anterior chamber in such eyes is enormously diminished. Wagenmann and Leber found that secondary glaucoma, with cupping of the disc, etc., arose in rabbits in which experimental irritation chanced to cause peripheral anterior synechia. Heisrath and Bentzen subsequently succeeded in producing a traumatic adhesion of the periphery of the iris to the cornea in rabbits; it was followed by persistent high tension and the usual sequelæ of this condition.

FIG. 690.—PRIESTLEY SMITH'S INJECTION APPARATUS.

Simpler apparatus for demonstrating the escape of fluid from the excised eye when the aqueous and vitreous pressures are equal (A), and its non-escape when the vitreous pressure is a little higher than that of the aqueous (B).

It is à priori improbable that any excretion of fluid from the anterior chamber takes place through ordinary lymph-channels, for it would be as difficult to conceive how the intra-ocular tension could then be maintained as on the theory of an open communication with the

veins. Experimental investigation confirms the absence of this mode of outflow, for even if the vessels are filled with a gelatinising material, so that they are completely blocked, or if the veins are tied, no distension of lymph-vessels is seen and filtration is abolished.

SCHWALBE.—A. f. mikr. Anat., vi, 1870. LEBER.—A. f. O., xix, 2, 1873; xli, 1, 1895. HEISRATH.—A. f. O., xxvi, 1, 1880. PAGENSTECHER.—B. d. o. G., 1878. GIFFORD.—A. f. A., xxvi, 1893. GUTMANN.—A. f. O., xli, 1, 1895. LEBER AND BENTZEN.—A. f. O., xli, 1 and 3, 1895. NUEL.—Internat. Congress, Utrecht, 1899. NUEL AND BENOÎT.—A. d'O., xx, 1899. ASAYAMA.—A. f. O., li, 1, 1900. PATERSON.—Jl. of Path. and Bac., 1904. LAUBER.—Merkel and Bonnet, Anat. Hefte, 1901. PRIESTLEY SMITH.—Glaucoma, London, 1879, 1891; Ophth. Rev., vii, 1888. KNIES.—A. f. O., xxii, 3, 1876; xxiii, 2, 1877. AD. WEBER.—A. f. O., xxiii, 1, 1877. WAGENMANN.—A. f. O., xxxiv, 1, 1888. LEBER.—Die Entstehung der Entzündung, Leipzig, 1891. HEISRATH.—C. f. d. med. Wissensch., 1879. BENTZEN.—A. f. O., xli, 4, 1895. HENDERSON AND STARLING.—Proc. Roy. Soc., B. lxxvii, 1906.

The part played by the iris and ciliary body in the excretion of aqueous is difficult to prove beyond dispute. In the dead eye after injection of carmin the coloured fluid passes out, not only by the anterior ciliary veins, but also in smaller quantity and less constantly by the vortex veins. Experiments on the living eye long failed to adduce definite proof of absorption by the iris. The injection of diffusible substances is useless for the purpose, and injection of Indian ink, etc., is liable to set up fibrin formation in the anterior chamber, which leads to the abstraction of the particles of ink. Staderini and others concluded that absorption did not occur, whilst the researches of Brugsch and Tückermann, under Leber's supervision, failed to give uncontrovertible results. Leber and Bentzen's experiments on the dead eye with Berlin blue gave evidence of absorption by the anterior surface of the iris and ciliary body, and pointed to excretion by filtration into the veins rather than by lymph-channels.

Nuel and Benoît and Asayama, by improved methods, using very small quantities of fluid, have succeeded in placing the matter beyond dispute. The former observers injected Indian ink into the vitreous in various animals, and in a few cases before enucleation in man, the eyes being removed from two and a half to six hours afterwards, when the ink had already passed into the anterior chamber. Asayama injected the fluid into the anterior chamber of rabbits, using special precautions against the loss of aqueous. Injection into the vitreous has the advantage that the hyaloid membrane and zonule filter off the larger particles, allowing only the very finest to pass forwards.

It is found that the inky fluid is absorbed by the whole of the anterior surface of the iris, but especially at the situations where crypts are most numerous—i. e. at the ciliary, and near the pupillary margins. The absence of endothelium here (Fuchs, Nuel and Cornil) doubtless facilitates absorption, permitting the particles to penetrate deeply into the stroma, the first serious resistance to their further progress being caused by the smooth muscle anterior to the retinal epithelium. In man the ink is found specially aggregated around the vessels in the middle layer of the iris, forming black rings round the veins and capillaries, whilst the arteries remain free. In favourable cases the ink can be seen inside the smaller veins and capillaries.
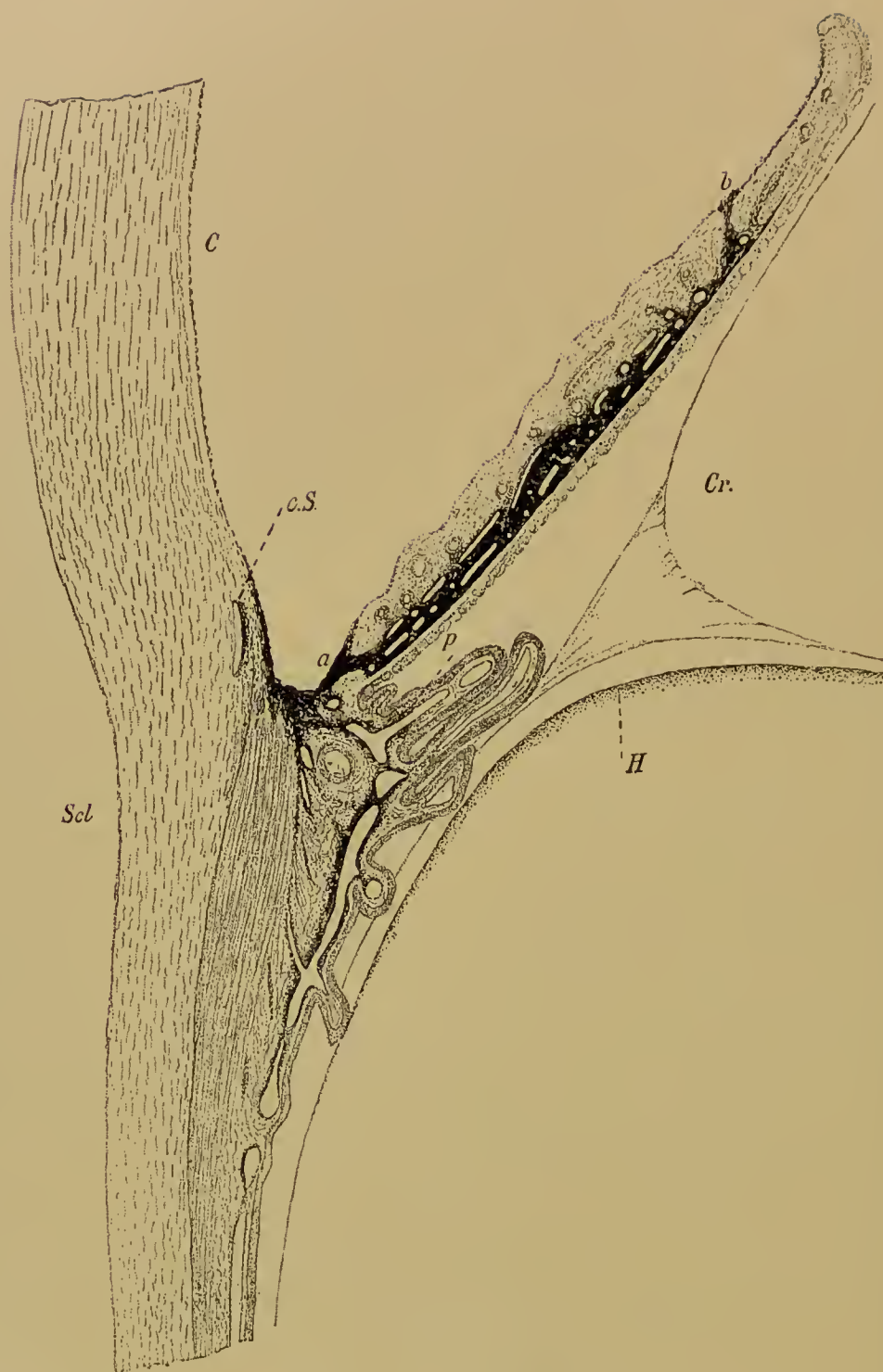
FIG. 691.—INDIAN INK IN THE IRIS, ETC.

After Nuel and Benoît, A. d'O., xx, 1900.   Indian ink was injected into the
vitreous of a child, æt. 5, two hours before enucleation of the eye.   From a bleached
section.   *C.* Cornea.   *Scl.* Sclerotic.   *c.S.* Canal of Schlemm.   *a.* Indian ink in
the periphery of the iris.   *b.* In the stroma near the pupillary margin.   *Cr.* Lens.
H. Hyaloid membrane.

The ink also accumulates in the anterior part of the ciliary body close to the angle, and is continued as a black sheath in the adventitia of the veins. Asayama traced the particles in flat preparations along the affluents of the vortex veins in the anterior part of the choroid, and even in the lumen of the vortex vein as it traversed the sclerotic. The excretion appears to take place therefore through the veins, and not by the perivascular channels.

The preponderant part played by the canal of Schlemm as compared with the iris and ciliary body is open to no doubt. This is shown by the far greater ease with which the anterior ciliary veins become injected, by the failure of filtration when the pressure in the vitreous exceeds that in the anterior chamber, the iris still remaining available for excretion processes, and by the abolition of filtration in secondary glaucoma, when the angle is blocked.

STADERINI.—A. f. O., xxxvii, 3, 1891. BRUGSCH.—A. f. O., xxiii, 3, 1877. TÜCKERMANN.—A. f. O., xxxviii, 3, 1892. BENTZEN AND LEBER.—A. f. O., xli, 3, 1895. NUEL AND BENOÎT.—A. d'O., xx, 1899. ASAYAMA.—A. f. O., li, 1, 1900. FUCHS.—A. f. O., xxxi, 3, 1885. NUEL AND CORNIL.—A. d'O., x, 1890.

The outflow of fluid from the vitreous is slow under normal conditions, as is shown by the results of injection experiments with fluorescein, etc. Probably under these circumstances all the lymph passes out by means of the perivascular sheaths of the central retinal vessels. If the anterior chamber is opened there is no question that the fluid finds an easy path forwards. It was early shown that if an eye is hung up by the optic nerve after a paracentesis almost all the fluid in the vitreous drains away, and the globe becomes quite flaccid (Janin, 1788). There can be no doubt that the restoration of the anterior chamber during life is largely aided by fluid passing forwards from the vitreous (Deutschmann); the fact has, indeed, been proved by Leplat's experiments with potassium iodide and Ovio's with strychnin, where these reagents were injected into the vitreous; the new aqueous after paracentesis contained appreciable quantities of the substances, derived obviously from the vitreous.

Schwalbe proved the permeability of the zonule for Berlin blue by showing that when it was injected into the anterior chamber it made its way into Petit's canal and to the back of the lens. Priestley Smith, on the other hand, proved the permeability of the hyaloid membrane and zonule for fluids passing from behind forwards. He connected cannulæ with the anterior and vitreous chambers; if fluid was injected into the latter at a higher pressure than obtained in the former the fluid ran out of the anterior cannula, having freely passed through the hyaloid and zonule. Still more striking are the researches of Nuel with Indian ink injected into the vitreous (v. p. 991).

It is improbable, however, that this path is used under normal conditions, for here the pressure in the vitreous and anterior chambers is equal; moreover, the ciliary body with its active secretory stream is interposed.

Schwalbe (1872) first demonstrated the connection of the central canal of the vitreous with the perivascular lymph-sheaths of the central

retinal vessels, and assumed this as an excretory path for the vitreous. Stilling adduced further proofs of the accuracy of the view, but over-estimated the importance of the path. Priestley Smith, by injecting fluid into the vitreous from a manometer, which stood at a pressure 10—15 cm. higher than a similar one connected with the anterior chamber, showed for the excised sheep's eye that scarcely any fluid passed into, and therefore out of, the eye. The lens and iris were by this means pressed against the cornea so that the filtration angle was blocked, the posterior exit by way of the optic nerve being alone available for excretion. He concluded that not more than $\frac{1}{50}$ part of the volume of fluid which passes out by the angle is excreted by this channel. Niesnamoff arrived at a similar proportion ($\frac{1}{55}$) by a different method. He covered the anterior part of the eye with collodion, so that the excretory channels here were blocked—under normal pressure with the pig's eye only about $\frac{1}{5}$ c.mm. was excreted per minute. If, on the other hand, the optic nerve and venæ vorticosæ were tied, and the posterior part of the globe was covered with collodion, no perceptible difference in the rapidity of excretion was observed. Schöler, too, could find no difference on tying the optic nerve.

Stilling, by tying the optic nerve, taking care to avoid injury to the posterior ciliary nerves, observed anæsthesia of the cornea and high tension. Russi in the rabbit, Marckwort and Ulrich in the dog, and Leplat have been unable to confirm this result.

The part played by diffusion in injection experiments must be carefully borne in mind. Thus Stilling, five minutes after injection of potassium ferrocyanide into the peritoneal cavity, found that the cut end of the optic nerve turned blue with ferric chloride, though the experiment failed to give a positive result after half an hour. It is noteworthy that in the rabbit, after tying and cutting the optic nerve, injection of fluorescein uniformly caused green coloration of the disc, though not of the opposite disc, nor after section alone.

Leplat's experiments with potassium iodide only prove the pro-duction of lymph from the ciliary body, not its excretion by the optic nerve, the question of diffusion again coming into play. He found that at intervals after the injection the amount of iodide in the vitreous diminished from before backwards, so that finally it could only be found in the posterior part. This is due to diffusion, the iodide passing back into the ciliary vessels when the quantity within them becomes less than that in the surrounding vitreous. Leplat opposed this view by argument that it would be a case of absorption by the vessels which secreted the fluid. It is not, however, a case of true absorption, but simply of physical diffusion (Leber).

The critical proof of this path of excretion is to be found in the results of injection of Indian ink. Ulrich and Gifford's earlier experi-ments were not conclusive. They found that the ink passed out by the perivascular sheaths, but the time which had elapsed was sufficient to allow of transmission by leucocytes. Later experiments by Ulrich on the rabbit are quite conclusive, the time necessary being only one and a half hours. These results have been confirmed by Nuel and Benoît, Leber, Paterson, and others.

JANIN.—Mém. et Obs. anat., physiol. et phys. sur l'Œil; Deutsche Uebers., Berlin, 1788. DEUTSCHMANN.—A. f. O., xxv, 1, 1879. LEPLAT.—Ann. d'Oc., xcvii, 1887. OVIO.—Sixth Internat. Congress, 1895. SCHWALBE.—A. f. mikr. Anat., vi, 1870. PRIESTLEY SMITH.— Ophth. Rev., vii, 1888. SCHWALBE.—Berichte d. k. sächs. Ges. d. Wiss. zu Liepzig, 1872. STILLING.—B. d. o. G., 1877, 1885; A. f. A., xvi, 1886. NIESNAMOFF.—A. f. O., xlii, 4, 1896. SCHÖLER.—A. f. O., xxv, 4, 1879. RUSSI.—Dissertation, Berne, 1880. MARCKWORT. —A. f. A., x, 1881. ULRICH.—A. f. A., xvii, 1887. LEPLAT.—Ann. d'Oc., xcviii, 1887. ULRICH.—A. f. O., xxx, 4, 1884; A. f. A., xx, 1889. GIFFORD.—A. f. A., xvi, 1886. BENOÎT, LEBER.—Internat. Congress, Utrecht, 1899. NUEL AND BENOÎT.—A. d'O., xx, 1899. PATERSON.—Jl. of Path. and Bact., 1904.

The perichoroidal space drains into the perivascular lymph-spaces around the vortex veins, as shown by Schwalbe (1868); he also showed that the injection mass sometimes passes along the posterior ciliary vessels, but that the intervaginal space of the optic nerve was never injected. v. Michel confirmed his observation that the perichoroidal space could be injected from Tenon's capsule when this itself was filled by injection into the subdural space of the brain, the mass flowing along the intervaginal space of the nerve; this only occurs in lower mammals —calf, sheep, pig, dog—not in man. Key and Retzius showed that in man the fluid passed from the intervaginal space into the perichoroidal space, and thence out into Tenon's capsule. Deutschmann asserts that once in a young rabbit, after injection of a few drops of Indian ink into the subdural space of the brain, he saw ophthalmoscopically the pigment pass from the edge of the disc into the perichoroidal space. Birnbacher and Czermak found that fluid injected into the perichoroidal space passes into the vortex veins, not into their perivascular sheaths. Leber, however, has fully confirmed the experiments of Schwalbe, which have further been supported by many other observers; it is, therefore, certain that the main outflow from the perichoroidal space is by way of the perivascular sheaths of the vortex veins. The lymph which passes by this route is small in quantity and is derived solely from the choroid and ciliary body, involving only the internal economy of these structures and having nothing to do with the maintenance of the intra-ocular pressure.

SCHWALBE.—C. f. d. med. Wissensch., 1868, 1869; A. f. mikr. Anat., vi, 1870. v. MICHEL. —A. f. O., xviii, 1, 1872. KEY AND RETZIUS.—Studien, Stockholm, 1875. DEUTSCHMANN. —Ueber die Ophthalmia migratoria, 1889. BIRNBACHER AND CZERMAK.—A. f. O., xxxii, 2 and 4, 1886. *LEBER.—In G.-S., 1903.

CHAPTER XVIII

THE NUTRITION OF THE EYE

THE CORNEA.

THE metabolism of the cornea is extremely slow. As an optical surface concerned in the refraction of rays of light entering the eye it performs its functions without any expenditure of energy. The chemical changes taking place in the fibrillæ which make up the substantia propria are minimal, as they are in fibrous tissue elsewhere in the body. Only the cellular elements—the epithelium, endothelium, and fixed corneal corpuscles—and the nerves demand nutritive supplies for the exhibition of their respective functions.

The maintenance of the transparency of the cornea involves no expenditure of energy. The cornea can be separated for more than half its circumference from the sclerotic without its transparency becoming impaired. Even small portions may in animals be entirely separated, yet on being replaced they will re-unite under favourable circumstances without loss of transparency (Wagenmann). If the cornea is stretched by pressure of air and allowed slowly to dry it remains transparent. The same occurs if the anterior chamber is kept filled with air (Coccius), even for several days; hence it follows that the aqueous is not essential for the nutrition of the cornea, though it cannot be asserted that it plays no part in the process. That diffusion occurs between them is undoubted, though, as will be seen later, under normal conditions there is no interchange of fluid, or if any interchange takes place it is in equivalent volumes. As has been already mentioned, Leber showed that the endothelium on Descemet's membrane protected the substantia propria from the absorption of water from the aqueous, even under artificial intra-ocular pressures far above those met with in pathological conditions—up to 200 mm. Hg. This observation is confirmed if the cornea is carefully removed, tied over the end of a glass tube, and an attempt made to force water, saline solution, etc., through it from the posterior surface. If, under similar circumstances, the endothelium is removed the fluid readily passes into the substantia propria with very low pressures, the lamellæ become swollen and opaque, and the epithelium is raised into vesicles, or if it has been removed the fluid appears in the form of drops upon the surface. If the endothelium is removed over limited areas, the opacification extends

only very slightly beyond the affected parts, so that the endothelium protects only the overlying portion.   Similar experiments can be performed on the living eye in animals, the endothelium being injured by the bend of a sharp hook introduced into the anterior chamber.   Similar absorption of fluid from the aqueous occurs when the endothelium is injured by pathological processes—*e. g.* interstitial keratitis (q. v.) (Mellinger, Bärri, E. v. Hippel).   It also occurs in corneal affections produced artificially by inhalation of ethyl chloride (Dubois, Panas), by insertion of the excised eye into the peritoneal cavity (Bullot and Lor), etc.   Softening and ectasia of the cornea may ensue during life from prolonged impairment· of the endothelium.   The demonstration of defects in the endothelium by fluorescein has already been referred to
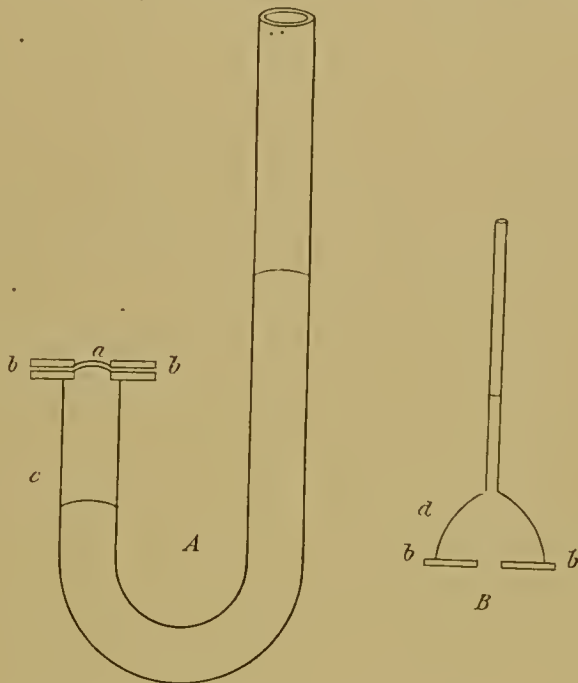
Fig. 692.—Leber's Filtration Apparatus.

A. For filtration against air.   *a.* Membrane, *e. g.* Descemet's or lens capsule. *b.* Perforated glass plates for fixing membrane.   *c.* Filtration fluid, with mercury below and in the other limb of the U-tube.   *B.* For filtration against fluids.

(*v.* Vol. I, p. 194).   It is due to *post-mortem* changes in the endothelium that some time after death droplets of fluid appear on the surface of the cornea, a fact which early observers wrongly attributed to the presence of pores through which the aqueous passed.

It is placed beyond dispute that Descemet's membrane offers no resistance to the passage of fluid by filtration.   v. Wittich in 1856 succeeded in filtering an albuminous fluid through the membrane under pressure, and Leber in 1873 confirmed this result with 0·75 per cent. NaCl solution on the intact membrane.   The filtration is not entirely abolished by leaving the endothelium, but this is due to unavoidable injury whereby the cells are brushed off in places.   The experiments are best performed with a U tube, the membrane being fixed over one end by clamping between two glass plates having a

4 mm. circular aperture. Koster, who repeated the investigations, thought that the passage of fluid might be attributed to injury to the membrane, but this is improbable. The presence of pores in Descemet's membrane, asserted by Preiss, has been disproved by Leber, who was unable to find any trace of them with the highest magnification after treatment with ferrous sulphate followed by potassium ferricyanide.

The inflow of fluid to the cornea from the marginal loops of vessels must be minimal, for they may be separated by a shallow circular incision just internal to them without any deleterious effect upon the cornea, other than that associated with healing of the wound. There is no actual flow of fluid, such as has been described by various authors; thus Gruber failed to find evidence of any afferent or efferent channels, with the possible exception of spaces around the marginal loops. The possibility of inflow from the marginal loops and outflow into the anterior chamber is opposed by the fact that fluid passes through Descemet's membrane only under a certain pressure, and in this case the substantia propria is on the negative side of the membrane. Moreover, it is improbable that the endothelium would allow fluid to pass from before backwards whilst blocking it in the reverse direction.

Pflüger found that if a linear abrasion was made in the cornea of a living animal and it was then stained with fluorescein, the green coloration spread in a sector towards the centre of the cornea, whilst it remained localised at the periphery; he attributed this to a flow of fluid inwards. Careful repetition of the experiments by Ehrenthal, Gifford, and Leber have failed to confirm the observations.

The popular view of such an inflow doubtless originates in the phenomena of diffusion which occur with foreign substances, and which have nothing to do with an actual flow of fluid (v. infra).

COCCIUS.—Die Ernährungsweise der Hornhaut, etc., 1852. LAQUEUR.—C. f. d. med. Wissensch., 1872. LEBER.—A. f. O., xix, 2, 1873; in G.-S., 1903. MELLINGER.—A. f. O., xxxvii, 4, 1891; Beiträge z. Augenheilkunde, Basel, 1893. BÄRRI.—Dissertation, Basel, 1895. E. v. HIPPEL.—B. d. o. G., 1898; A. f. O., liv, 1902. DUBOIS, PANAS.—Comptes rendus, cvii, 1888. BULLOT AND LOR.—Bull. de l'Acad. de Méd. de Belgique, 1899. BULLOT.—Thèse de Bruxelles, 1901; Jl. of Phys., xxxi, 1904. v. WITTICH.—Virchow's Archiv, x, 1856. KOSTER.—A. f. O., li, 2, 1900. PREISS.—Virchow's Archiv, lxxxiv, 1881; lxxxvii, 1882. GRUBER.—A. f. O., xl, 4, 1894. PFLÜGER.—K. M. f. A., xx, 1882. EHRENTHAL.—Dissertation, Königsberg, 1887. GIFFORD.—A. f. A., xxvi, 1893.

The normal cornea contains a large percentage of water—man, 76·6 per cent. (His); ox, 78·9 per cent. (Leber). After immersion in distilled water the percentage may rise to 94·7 in one day, 96 after four days; this is accompanied by great swelling, the thickness increasing eight times the normal, and the weight four to five times (Leber). Similar results have been obtained by Chevreuil, Coccius, L. Meyr, and Donders. Aqueous, normal saline solution, etc., give slightly smaller, though not essentially different, results, and it is not necessary that the fluid should be isotonic, for the dead cornea, like other dead tissues, readily absorbs water from strong saline solutions—e.g. 10 per cent. NaCl (Schweigger-Seidel).

Bowman long ago pointed out that the amount of water in the cornea is only that sufficient to maintain the tissues moist, there being absolute contact between the structural elements. The absorbed water

is in a condition of physical, though not chemical, combination. Leber found that under high pressures, of 50—350 atmospheres, with a Buchner's press, much of the fluid can be expressed. With seventy-four ox and calf corneæ only 2 c.c. were obtained. Most of the fluid was pressed out at 50—100 atmospheres. In order to obtain the maximum the corneæ must be minced and mixed with kieselguhr, a finely divided powder consisting of diatoms. Twenty grammes of ox cornea gave the following percentages : expressed fluid, 16·41 per cent. ; water after drying at 100°, 62·51 per cent.—i. e. total water, 78·92 per cent. ; dry substance, 21·07 per cent. Hence only one fifth of the water can be pressed out. The specific gravity of the fluid was 1·0074, in the later stages of expression 1·010. This value compares very accurately with that of ox aqueous, 1·0076—1·0086 (Michel and Wagner). The same applies to the refractive index, 1·336—1·338, as compared with 1·338 for aqueous (Cyon) ; it is higher for the cornea in man, 1·372—1·377 (Aubert and Matthiessen).

The chemical characteristics of the fluid also very closely resemble those of aqueous. It contains an albumin, coagulating at 68°—70°, and a globulin, coagulating at 75°. There is no spontaneous coagulation. Mörner's mucoid is present in larger quantity than in aqueous, where it is found only in the smallest traces ; it is a true mucin, giving a sugar reaction after heating with 5 per cent. sulphuric acid, and is doubtless derived from the cells. There is a trace of diastatic ferment, but no peptonising ferment.

The resemblance of the fluid to aqueous is not surprising, and does not involve the conclusion that the aqueous is directly transferred to the cornea. The low metabolism of the cornea necessarily results in equalisation of crystalloid constituents by diffusion.

Fluid can easily be pressed out of the swollen cornea under very low pressure. The water is not, however, contained in preformed spaces, but the cornea behaves like any other gelatinous material, though with the latter higher pressures are requisite.

LEBER.—A. f. O., xix, 1873.

The fibrillæ of the cornea, like those of other connective tissues, are normally in a state of tension, which differs in the axial and transverse directions, a difference which manifests itself physically in optical double refraction. When the tissues absorb water there is a tendency to equalisation of tensions, associated with approximation to the spherical form. This results in alteration in shape of the cornea, whereby it becomes thicker whilst its superficial area becomes diminished, and also in loss of double refraction. His pointed out that the strongly swollen cornea, as, for example, after heating with water, ceases to be doubly refracting.

It is the double refraction attendant upon increased tension of the fibrillæ which causes the haziness of the cornea in the glaucomatous state (v. Fleischl). The increased double refraction necessarily leads to stronger reflection at the surface of each fibril as the light passes from one to another within the cornea ; hence the breaking up of the light rays, which manifests itself as a diffuse haze. Under normal

conditions, though the fibrils are slightly doubly refracting, as shown by examination of the fresh normally curved cornea with crossed Nicol prisms (His, v. Ebner), yet the optical effect is diminished and compensated by the fact that the fibrils run in every possible direction. Bowman long ago pointed out that the condition was not due to absorption of water or so-called œdema. It is, indeed, independent of the presence of aqueous, since it occurs equally well if the anterior chamber is filled with air or if the cornea is tied over the end of a tube.

On removal of the pressure the haze disappears immediately, a fact which cannot be explained by the absorption of water. L. Meyr found that the ox eye became hazy under a tension of 150 mm. Hg, but Leber found that it was not very marked under less pressures than 200 mm. Hg.

His.—Beiträge zur norm. u. path. Histologie der Cornea, Basel, 1856. Chevreuil.—In Liebig, Untersuchungen, Braunschweig, 1848. Coccius.—Die Ernährungsweise der Hornhaut, etc., 1852. L. Meyr.—Ueber die Trübungen der Hornhaut, München, 1856. Donders.—A. f. O., iii, 1, 1857. Schweigger-Seidel.—Berichte d. sächs. Ges. d. Wiss zu Leipzig, 1869. Bowman.—Lectures on the Parts concerned in Operations on the Eye, London, 1849. v. Michel and Wagner.—A. f. O., xxxii, 2, 1886. Aubert.—In G.-S., ii, 1876. Mörner.—Z. f. physiol. Chemie, xviii, 1893. Lépine.—Berichte d. sächs. Ges. d. Wiss zu Leipzig, xxii, 1870. Leber.—A f. O., xix, 2, 1873; in G.-S., 1903. v. Fleischl.—Sitzungsberichte d. Wiener Akad. d. Wissensch., lxxxii, 1880. v. Ebner.—In Kölliker's Handbuch der Gewebelehre, iii, 1902.

The question of preformed channels in the cornea has given rise to much discussion. Impregnation with silver demonstrates a network which v. Recklinghausen thought were canals—v. Recklinghausen's canals (Saftkanälchen)—and he considered that the observation confirmed Virchow's view of a system of channels filled with plasma and destined for the nourishment of the cornea. There is no doubt that these positive impregnation pictures, such as are obtained with gold and with special silver methods, are due to the strongly reducing action of the nerves and fixed corpuscles. They do not prove the existence of channels, and this is still less effected by negative impregnation pictures such as are usually obtained with silver, and always with ferrous sulphate and potassium ferricyanide, ferrous or cuprous sulphate and ammonium sulphide, lead acetate and potassium birchromate, etc. Here the intercellular substance alone is stained, the cells and nerves remaining clear. The two methods do not give completely accordant results, the negative picture showing wider spaces and coarser processes.

More stress must be laid upon the results of injections into the cornea. By the injection of air or mercury Bowman demonstrated a system of tubules—Bowman's corneal tubes; watery solutions are not well suited for the purpose owing to the swelling of the tissues. v. Recklinghausen used coloured oily fluids, and Leber found turpentine coloured with alkanna particularly good. Oil followed by osmic acid also gives good results, and Gutmann used Retzius' fluid—a solution of asphalt in chloroform. The picture obtained with low pressures agrees entirely with that obtained by other methods of the corneal corpuscles and their processes. Higher pressures reveal spindle-

shaped spaces and tubules, every gradation being seen. The injection readily passes along the nerves.

These spaces are artificially produced by the pressure of injection. They communicate with the lymph-channels of the conjunctiva, which can be easily injected from them. The fluid also passes into the inter-cellular spaces of the epithelium (Leber), demonstrating well the channels between the spines of the prickle-cells. Turpentine oil is taken up by the epithelial cells in very fine droplets, which, however, do not invade the nuclei.

The presence of leucocytes in the cornea does not prove that there are preformed channels; the latter move merely in the direction of least resistance, which will naturally be along the lamellæ.

BOWMAN.—Lectures on the Parts concerned in Operations on the Eye, London, 1849. v. RECKLINGHAUSEN.—Die Lymphgefässe, 1862; Anat. Anzeiger, iii, 1888. LEBER.—K. M. f. A., iv, 1866; A. f. O., xiv, 3, 1868; xix, 2, 1873; xxiv, 1, 1878. GUTMANN.—A. f. mikr. Anat., xxxii, 1888. RÄHLMANN.—A. f. O., xxiii, 1, 1877. WALDEYER.—In G.-S., i, 1874. KRÜKOW AND LEBER.—A. f. O., xx, 2, 1874. SCHREIBER.—A. f. O., lviii, 2, 1904.

Absorption of foreign substances by the cornea from the surface or from the anterior chamber is impeded by the presence of the epithelium and the endothelium. It takes place only by diffusion, and is extremely slight in any case; nevertheless it is sufficient to produce profound physiological results, and has therefore to be taken into consideration.

Absorption from the anterior surface was first proved by de Ruiter and Donders in 1853 for atropin sulphate, confirmed by v. Graefe (1854). In 1855 Gosselin extended the observations to potassium iodide and calcium hydrate and in 1864 B. Rüte to eserin.

The effect with atropin is more rapid the thinner the cornea, and hence differs according to the age or species of the animal. It is much hastened by removal of the epithelium (v. Graefe). It occurs equally well when the solution is brought in contact with only an isolated portion of the cornea, other parts and the conjunctiva being carefully protected (de Ruiter, Wysotzky, Kisseleff). Most conclusive are the experiments of de Ruiter in which the aqueous is removed with all precautions after instillation of atropin and then dropped into a normal eye. This aqueous acts like a solution of atropin of the strength of 1 : 120,000; it gives the physiological effect upon the pupil, but at the same time demonstrates the small amount of diffusion which takes place. Positive results are obtained by the same method with eserin (B. Rüte, Wysotzky, Lilienfeld). Atropin and eserin instilled into the eye immediately after death cause their characteristic effects upon the pupil, so that there is no question of absorption into the conjunctival blood-stream (Schöler, Laqueur).

The absorption of strychnin nitrate from a 1 per cent. solution is proved by the onset of tetanic symptoms (Lilienfeld). Potassium iodide, after five to eight instillations of 10 to 20 per cent. solution in the rabbit, can be detected in the cornea in one and a half minutes, in the aqueous in two minutes, by testing with nitric acid and starch (Gosselin): the palladium chloride test is more convenient and more delicate. Sodium salicylate is absorbed by the rabbit's cornea from a 10 per cent. solution (Ulry and Frézals).

The effect is more pronounced in the excised eye: thus, in the living rabbit after free instillation of 5 per cent. ferricyanide of potassium no trace is found in the aqueous unless the epithelium is removed. That it is absorbed is shown by the possibility of detecting it in the urine. In the excised eye it can be detected in the aqueous, even when the epithelium is intact (Krükow and Leber; *cf.* Gosselin, Memorsky, Laqueur, Bellarminoff).

The hindrance to absorption afforded by the epithelium is best exemplified by the effects of methylene blue (Bullot and Lor) and fluorescein (Pflüger, Straub, Bellarminoff). In the former case the dye is absorbed only where the epithelium is defective; the cornea is stained diffusely, the corpuscles not at all, so that a negative picture is obtained. The effects of fluorescein are familiar from its use clinically.

The deleterious effect of certain substances upon the epithelium must therefore be taken into account. Thus, absorption is very rapid with concentrated saline solutions; the accumulation of salts in the aqueous may be so great that water is abstracted from the lens, which becomes opaque (Heubel). The effects of iodine, alcoholic solutions of potassium iodide, strong solutions of copper sulphate, ferric chloride, etc. (Lilienfeld), are due rather to the destruction of the epithelium than to the inflammatory hyperæmia of the conjunctiva.

Calcium hydrate has a specific effect; it is absorbed in the soluble state and deposited in the cornea as carbonate (Gosselin, de Gouvea). Absorption is aided by the caustic action upon the epithelium, and this may extend more deeply, leading to softening and necrosis. If the cornea is not destroyed it assumes a porcelain-like appearance: the presence of carbonate is demonstrated by the evolution of gas on the addition of acids.

The effects of cocain are also complex in their origin. Besides the deleterious action upon the epithelium (*v.* Vol. I, p. 203) the paralysis of the sensory nerve endings has to be taken into account. The insensibility of the cornea leads to drying, and also to absence of blinking and diminished secretion of tears. Würdinger found in the rabbit, not only unevenness and other changes in the epithelium, such as are seen after section of the trigeminal nerve, but also thinning of the substantia propria, which can be due only to loss of water. On addition of fluorescein or methylene blue the whole parenchyma became stained. Schmeleff and Bellarminoff found the absorption of fluorescein increased by previous cocainisation; on unilateral application of cocain in man this action is masked owing to the blinking being symmetrical.

That the effect of cocain is not entirely due to drying is shown by Bellarminoff's experiments in which the cornea was kept moist. By a colorimetric method he showed that after cocain the absorption of fluorescein was increased threefold. The investigations of Laqueur, Koster, and Silfvast show a specific deleterious effect upon the epithelium in man and the rabbit when great care is exercised to avoid drying. The endothelium also suffers, as shown by Mellinger; after injection of 2 per cent. cocain and $\frac{1}{2}$ per cent. NaCl into the anterior chamber of a rabbit subcutaneous injection of fluorescein caused green coloration of the cornea, whilst the opposite cornea remained unstained.

Cocain probably has also an indirect effect, probably through its constricting action upon the conjunctival vessels. Bellarminoff has shown that cocain has no effect on the freshly dead eye ; moreover, in the living animal its effect is diminished by previous section of the sympathetic, whereby the vessels remain dilated. This aspect of the subject is complicated, and requires further investigation. Thus tropococain is said to have a vaso-dilator action (Andogsky), whilst still increasing diffusion like cocain (Annine).

Absorption from the anterior chamber takes place under similar conditions to that from the anterior surface, the endothelium offering the same resistance as the epithelium. Descemet's membrane apparently offers some resistance to diffusion. Many crystalloid substances pass through it very rapidly, others more slowly—e. g. fluorescein in one minute, methyl violet only after thirteen minutes, the membrane being deeply stained (Leber). Berlin blue does not pass through. Proteids pass through very slowly ; thus with blood-serum diffused against distilled water the latter shows a definite trace of proteids after one day, gradually increasing, but still slight after four days. Hæmoglobin passes through in still smaller quantity (cf. Vol. I, p. 249). Whether starch solution injected into the anterior chamber diffuses is open to doubt, since only traces of sugar can be recovered in the cornea (Knies, Gruber). Granular substances (e. g. Indian ink) are stopped by Descemet's membrane ; they are caught by the cement substance between the endothelial cells and also penetrate into the cells.

DE RUITER.—Dissertation, Traj. ad Rhen., 1853. V. GRAEFE.—A. f. O., i, 1, 1854. GOSSELIN.—Gaz. hebd., 1855. B. RÜTE.—A. f. Heilkunde, v, 1864. WYSOTZKY, KISSELEFF. —In Nagel's Jahresbericht, 1873. LILIENFELD.—Dissertation, Rostock, 1873 ; in Nagel's Jahresbericht, 1873. SCHÖLER.—Dissertation, Dorpat, 1869. LAQUEUR.—C. f. d. med. Wissenschaft, 1872. HILBERT.—In Nagel's Jahresbericht, 1883. ULRY AND FRÉZALS.— A. d'O., xix, 1899. KRÜKOW AND LEBER.—A. f. O., xx, 2, 1874. MEMORSKY.—A. f. O., xi, 2, 1865. BELLARMINOFF.—A. f. O., xxxix, 3, 1893. BULLOT AND LOR.—Bull. de l'Acad. de Méd. de Belgique, 1899. PFLÜGER.—K. M. f. A., xx, 1882. STRAUB.—C. f. A., xii, 1888. HEUBEL.—Pflüger's Archiv, xx, 1879. DE GOUVEA.—A. f. A., i, 1869. WÜRDINGER.— Münchener med. Woch., 1886. SCHMELEFF.—In Bellarminoff. LAQUEUR.—B. d. o. G., 1888. KOSTER.—Tijd. v. Geneesk., i, 1899. SILFVAST.—In Leber, G.-S., 1903. MELLINGER. —A. f. O., xxxvii, 4, 1891. ANNINE, ANDOGSKY.—Ann. d'Oc., cxxvi, 1901. KNIES.— Virchow's Archiv, lxii, 1875. GRUBER.—A. f. O., xl, 4, 1894.

The passage of substances from the blood-vessels into the cornea may be by three routes—from the fluid in the conjunctival sac, from the aqueous, or directly into the cornea. Of these the first may be dismissed as beyond the limits of probability, since the epithelium offers considerable resistance to absorption. In spite of the resistance offered by the endothelium it has already been shown that absorption takes place from the anterior chamber. Experiments have been carried out to determine whether foreign substances injected into the blood appear sooner in the cornea or in the aqueous. Gruber employed an ingenious method. He introduced particles of iron wire into the cornea of cats at various positions and depths, thus causing the formation of rust spots. He then injected 1 per cent. ferrocyanide of potassium into the circulation, and found that in from eight to twenty-six minutes

the spots became blue whilst the aqueous remained uncoloured. He further noted that peripheral spots became stained sooner than those more centrally situated. Leber obtained similar results with potassium iodide. Laqueur, however, found that the same earlier staining of the periphery occurred when ferrocyanide of potassium was introduced into the aqueous; thus if a radial abrasion was made in the epithelium and ferric chloride applied the peripheral part of the streak stained before the central. Leber's researches with potassium iodide seem incontestably to confirm Gruber's deductions, viz. that the substance passes first into the cornea and only later appears in the aqueous. The endothelium in the early stages gives no reaction for iodine, whilst the corneal substance stains distinctly after the endothelium has been brushed off; at the same time the aqueous contained much iodide, thus showing how great is the resistance of the endothelium to diffusion. If the epithelium and endothelium are removed, the iodine is more concentrated in the posterior layers of the cornea than in the anterior; at a later stage it is equally diffused, and finally it is less concentrated behind than in front.

Leber, after internal administration of 1—2 gm. of potassium iodide to rabbits, obtained a negative impregnation picture on treating with palladium chloride fifteen minutes later, the epithelium or the endothelium being gently brushed off. Sometimes the reaction occurred in the posterior layers and not in the anterior. At a slightly later stage the endothelium showed punctate deposits and staining of the lines of cement substance. Leber considers that this is due to the iodide being taken up by the endothelium from the aqueous.

Indigocarmin solution acts differently. J. Arnold found in the frog after prolonged injection by the circulation that the cement substance between the epi- and endothelial cells became stained, the latter especially if a thread was drawn through the cornea and the conjunctival sac was irrigated with 1·5 per cent. NaCl. Both by this method and by injection of indigocarmin into the anterior chamber a positive, not a negative, impregnation picture is obtained. So too with Ehrlich's vital methylene blue method, not only the nerve-fibres but also the corneal corpuscles are stained (Hosch). There is, therefore, some specific reaction with these reagents dependent doubtless upon chemical combinations which are not fully understood.

In some forms of keratitis, and after ligature of the venæ vorticosæ, deposits of fibrin are found throughout the substantia propria (Leber). The whole cornea is then permeated with highly albuminous fluid. The fibrin is deposited as a fine network, and also in the form of rod-like or ovoid particles arranged in rows between the fibrillæ.

Anti-bodies also become diffused into the cornea as well as into the aqueous (Römer). Thus the corresponding antitoxins, injected subcutaneously in rabbits, are found to protect from the keratitis produced by the organisms of diphtheria and pneumonia and by the cocci of erysipelas in mice.

All these experiments tend to show that the metabolism of the cornea is carried out through filtration from the vessels and diffusion from the periphery, diffusion from the aqueous playing a subsidiary

part. They afford no support to the view that there are preformed lymphatic channels (Leber).

GRUBER.—A. f. O., xl, 4, 1894. LAQUEUR.—C. f. d. med. Wissenschaft, 1872. J. ARNOLD.—Virchow's Archiv, lxvi, lxviii, 1876. EHRLICH.—Deutsche med. Woch., 1886. HOSCH.—A. f. O., xxxvii, 3, 1891. LEBER.—A. f. O., xxxv, 1, 1889; in G.-S., 1903. RÖMER. —A. f. O., liv, 1, 1902; B. d. o. G., 1902.

The nutrition of the cornea is affected by changes in the ciliary circulation, both by cutting off the arterial supply and by impeding the venous return. If the long ciliary and most of the short ciliary arteries are cut in the rabbit, the endothelium becomes necrotic and is cast off, the substantia propria swells and becomes hazy, and fibrin is deposited (Wagenmann, Siegrist, E. v. Hippel). These changes are followed by proliferation of the corpuscles and vascularisation, pointing to some necrosis of the substantia propria. The early changes in the endothelium are shown by staining with fluorescein. The changes produced by tying the vortex veins are similar, but less pronounced (Koster). Owing to the increased intra-ocular pressure following this procedure the cornea may stretch and become ectatic (E. v. Hippel).

The explanation of the changes produced by section of the posterior ciliary arteries is difficult. They give no branches to the peripheral corneal loops, and the circulation here, derived from the arteries of the recti, is not interfered with. The long ciliary arteries are the most important, since section of the short ciliaries alone is without effect upon the cornea. Further, the corneal complications follow removal of the iris and ciliary body in the rabbit, which leaves the corneal loops intact, whilst, on the other hand, Ranvier's incision concentric with the corneal margin internal to the peripheral loops does not affect the transparency of the cornea. It would seem, therefore, that the injury is caused by interference with the circulation in the ciliary body, probably by affecting the composition of the lymph secreted. It is not due to accumulation of carbon dioxide, as might be thought from the positive result of ligature of the vortex veins, since filling the anterior chamber with this gas leads to no ill effect ; it is absorbed in less than twenty-four hours.

Deficiency of oxygen, on the other hand, has a distinctly bad effect upon the cornea, as has been well shown by Bullot and Lor's investigations. Fresh enucleated eyes of rabbits were introduced into the peritoneal cavity of another rabbit and the changes in the cornea observed. These varied according to whether the epithelium was previously removed or not ; in the former case the cornea remained clear and of normal thickness, in the latter it became cloudy and thickened. The cause of the changes is necrosis of the endothelium, which only occurs when the epithelium is intact. If the epithelium is partially removed the underlying endothelium is protected whilst the remainder necroses. These results are very well demonstrated by staining with borax carmin and methylene blue ; the epithelial abrasions stain red and the endothelial defects blue, so that a red patch corresponds with an unstained posterior area.

If the eye with intact epithelium is placed in a moist chamber, the cornea remains clear for twenty-four hours, so that the change is not due to deficient nourishment. If, however, the air in the chamber is gradually replaced by hydrogen in increasing quantity, it is found that the cornea becomes opaque just as in the peritoneal cavity when the atmosphere contains one seventh its volume of hydrogen. In pure hydrogen the endothelium necroses whether the epithelium is removed or not. The results are the same with local abrasions as in the body cavity.

Bullot concludes that the death of the endothelium is due to insufficient supply of oxygen, the epithelium preventing its entrance into the eye. The oxygen in the peritoneal cavity is probably not more than 3 per cent., viz. that of serum. With higher percentages of
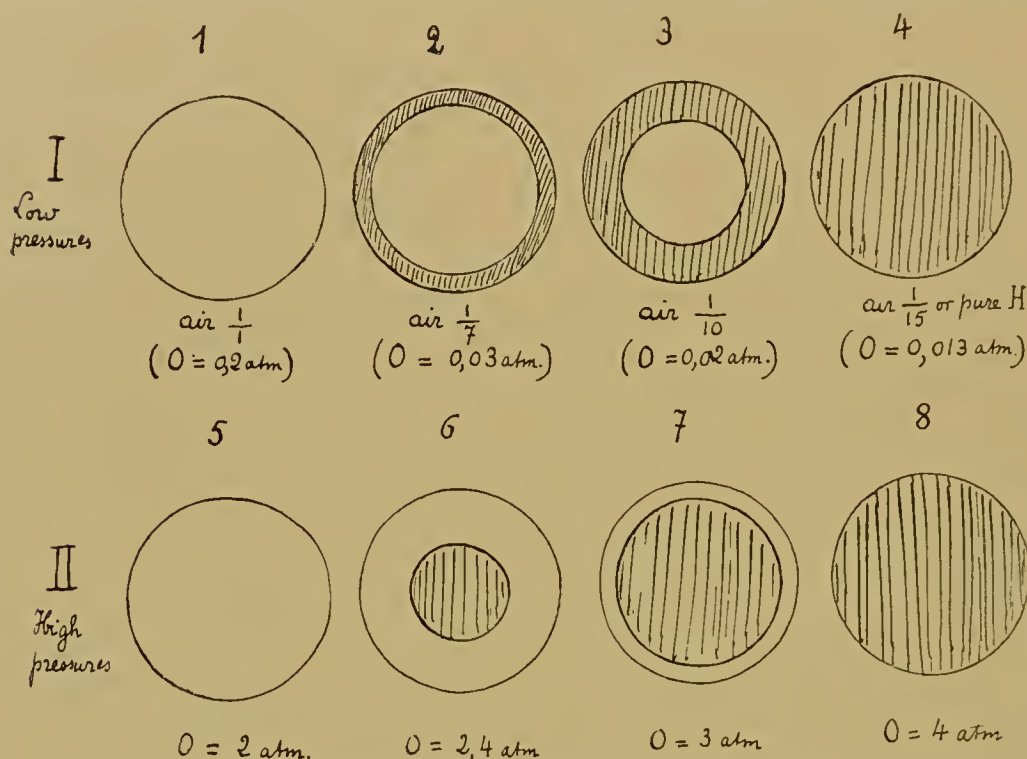
Fig. 693.—Action of Oxygen upon the Cornea.

Bullot, Journ. of Phys., xxxi. Aspect of posterior surface of rabbit's cornea when the entire eyeball has been kept for fifteen hours at 35° C. in oxygen at various pressures. The striated regions represent areas of dead endothelium. I. Low pressures. II. High pressures.

oxygen, as in pure air, sufficient passes through the epithelium to keep the endothelium alive. The supply in the body-cavity is enough to allow of regeneration of the epithelium over defects during the first two days, the inner parts of the eye dying rapidly owing to the absence of the blood circulation.

Bullot has further shown that if the eye with its epithelium scraped off is placed in an atmosphere of moist air at 35° C., after fifteen hours the endothelium is living over the whole posterior surface. If the atmosphere consists of one part of air to fourteen parts of hydrogen, which is equivalent to air rarefied to one fifteenth, the endothelium after the same length of time is found to be dead over the entire

surface (Fig. 693, I). When the air is less rarefied, only to one seventh or one tenth, the endothelium remains alive except over a circular zone at the periphery, which is wider the more the air is rarefied. Again, with increased pressures of oxygen, if the eye is kept in pure oxygen at one atmosphere pressure for fifteen hours, or even at two or 2·2 atmospheres, the endothelium remains alive over the whole area (Fig. 693, II). When the oxygen is compressed to 2·4 atmospheres, the endothelium is partly killed, but not at the periphery as with rarefied air, but in the centre within a sharply defined circular area. When the oxygen is compressed to three atmospheres, the circle of dead endothelium is broader, only a very narrow zone of living endothelium persisting at the periphery. Only when the pressure is increased to between three and four atmospheres is the endothelium killed *in toto*. From these experiments it follows that the peripheral endothelium, which is the first to be killed through insufficiency of oxygen, is the last to die from excess of oxygen, while the central endothelium, which is the last to die through insufficiency of oxygen, is the first to be killed when exposed to an excess of this gas. The explanation of these peculiarities is as yet unknown. The iris is of no account, since previous iridectomy or contact of the iris with the cornea makes no difference to the results. It is probable that the ciliary body plays no part, though this is not placed beyond dispute. It is not improbable that the endothelium is regenerated from the periphery, like the epithelium; if so, the phenomena might be explained on the teleological grounds that the periphery requires more oxygen and is therefore more resistant to excess and less resistant to an insufficient quantity.

Bullot found that if the epithelium is killed with chloroform it ceases to stop the oxygen; whether the normal epithelium is actually impermeable to oxygen or whether it simply absorbs the gas is not yet determined. It is certainly itself very resistant to diminished supply of oxygen, since it remains alive for fifteen hours in an atmosphere of almost pure hydrogen, and in a mixture of nine volumes of hydrogen to one volume of air regeneration will go on.

The clouding of the cornea which occurs after prolonged administration of ethylene chloride, first observed by Dubois, is probably due to necrosis of the endothelium (Panas). There is considerable conjunctival injection, with lacrymation and photophobia; the cornea becomes white like porcelain, and the pupil is dilated. The opacity, after a week or more, commences to clear from the periphery towards the centre; occasionally the cornea becomes conical. Microscopically there is necrosis of the endothelium and œdema of the substantia propria, the epithelium being normal. The condition may be induced also by subcutaneous injection or introduction into the anterior chamber, but not by the action of the vapour upon the cornea nor by instillations.

The keratitis which occurs rarely after extirpation of the thyroid gland is also probably due to necrosis of the endothelium. I observed it in one case in which I removed the thyroid in a dog, and it has been examined anatomically by Gley and Rochon-Duvigneaud. They found leucocytic infiltration, but made no special investigation of the condition of the endothelium.

A similar toxic keratitis, also probably due to interference with the vitality of the endothelium, is found sometimes after internal administration of naphthalin. The drying of the epithelium and cloudiness of the cornea following instillation of suprarenin (Wessely) resembles rather the effects of cocain already considered (v. p. 1002).

WAGENMANN.—A. f. O., xxxvi, 4, 1890. SIEGRIST.—A. f. O., l, 1900. E. v. HIPPEL.—A. f. O., liv, 1902. KOSTER.—A. f. O., xli, 2, 1894. BULLOT AND LOR.—Bull. de l'Acad. de Belgique, 1899. BULLOT.—Thèse de Bruxelles, 1901 ; Jl. of Physiology, xxxi, 1904. DUBOIS, PANAS.—Comptes rendus, cvii, 1888. GLEY AND ROCHON-DUVIGNEAUD.—Arch. de Phys. norm. et path., vi, 1894. PARSONS.—Jl. of Anat. and Physiol., xxxv, 1901.

THE LENS

The chemical constitution of the lens in the ox is as follows (Laptschinsky) :

	Per cent.
Water	63·50
Solids	36·50
Proteids	34·93
Lecithin	0·23
Cholesterin	0·22
Fats	0·29
Salts	0·82

It will be noticed that the proteid matter is very abundant ; it consists chiefly of a globulin, to which Berzelius gave the name crystallin. According to Mörner about 52 per cent. of the proteid matter of the lens is insoluble in water and saline solutions. The insoluble residue is an albuminoid, and it is most abundant in the nucleus. It yields no nuclein on gastric digestion. The soluble proteids are also not nucleins: about 1 per cent. consists of albumin, the remainder of globulin. The globulin resembles vitellin in being precipitated by saturation with magnesium sulphate, but not with sodium chloride. It consists of two proteids—α-crystallin, coagulating at 72° C., and β-crystallin, coagulating at 64° C. The former is more abundant in the outer, the latter in the inner portions of the lens; the albumen is equally distributed. The lens contains no keratin. The cholesterin is much increased in cataract (Cahn).

According to Deutschmann and W. J. Collins the human lens contains a considerably larger percentage of water than that of lower mammals. The percentage is about 70, but the observers do not agree as to the effect of age, Deutschmann finding a diminution in the amount of water in advanced life, Collins an increase. Their results are as follows :

Deutschmann :

Age in years.	Weight in grammes.	Percentage of water.	Percentage of dry solids.
3	0·149	70·84	29·16
32	0·190	70·60	29·40
35	0·199	69·91	30·09
40	0·191	70·50	29·50
42	0·179	68·30	31·70
63	0·223	64·63	35·37

W. J. Collins:

Age in years.	Weight in grammes.	Percentage of water.	Percentage of dry solids.	Ash.
10	0·163	69	31	0·6
26	0·215	71	29	0·9
27	0·188	72	28	0·5
28	0·192	69	31	1·0
40	0·218	73	27	0·4
64	0·247	71	29	0·4

The weight of the lens increases steadily throughout life, therein differing from all other organs of the body. E. v. Jäger gives the following determinations:

Age.	Mean weight in grms.
6—14 days	0·084
16—40 ,,	0·095
100 ,,	0·122
16—28 years	0·163
31—40 ,.	0·176
42—47 ,.	0·216
52—54 ,,	0·214
62—63 .,	0·233
72 ,,	0·279

It will be noticed that the weight at twenty years is about double that at birth, whilst from twenty to eighty years there is an increase of only about 30 per cent.

Priestley Smith's determinations agree well with those of v. Jäger, and he has shown further that the volume and equatorial diameter of the lens also steadily increase throughout life:

Age in years.	Weight in grammes.	Volume in c.mm.	Specific gravity.	Equatorial diameter in mm.
20—29	0·174	163	1·067	8·67
30—39	0·192	177	1·085	8·96
40—49	0·204	188	1·085	9·09
50—59	0·221	205	1·078	9·44
60—69	0·240	225	1·067	9·49
70—79	0·245	227	1·079	9·64
80—90	0·266	244	1·090	9·62

In these experiments the volume of the lens was determined by an apparatus in which the displacement of rectified oil of turpentine in a graduated and calibrated tube is measured (Fig. 694). The specific gravity was calculated from the weight and volume. Priestley Smith points out that between twenty-five and sixty-five years of age the lens adds about one third to its weight, one third to its volume, and one tenth to its diameters. The specific gravity appears to vary a little in individual cases, but shows no decided change with advance of life. Lenses that are becoming cataractous are as a rule smaller than healthy lenses of the same period of life (Fig. 695). The physiological explanation of these facts is to be found in the origin and nature of the lens. It is derived from the cuticular epiblast, and is analogous in its mode

of growth to the cuticle. Its cells, unlike those of the cuticle, are not cast off as they grow old ; they are laid down layer by layer within a closed capsule, the younger fibres surrounding the older. In consequence of this unique arrangement, and in spite of the shrinking of the older cells which form the nucleus, the growth of the lens does not cease with that of the rest of the body, but is continuous throughout the whole period of life. In advanced life the process of growth often fails; then the shrinking nucleus tends to separate from the softer cortex, and senile cataract begins. Hence the lens with incipient cataract is usually smaller than the healthy lens of the same age. The swelling of the cortex which takes place during the development of the cataract may counteract this effect.

LAPTSCHINSKY.—Pflüger's Archiv, xiii, 1876. CAHN.—In Hoppe-Seyler, Physiologische Chemie, iii, 1881. v. MICHEL AND WAGNER.—A. f. O., xxxii, 2, 1886. MÖRNER. —Z. f. physiol. Chemie, xviii, 1893. DEUTSCHMANN.—A. f. O., xxv, 2, 1879. W. J. COLLINS.—Ophth. Rev., viii, 1889. E. v. JÄGER.— Ueber die Einstellungen des dioptrischen Apparates, Wien, 1861. PRIESTLEY SMITH.—R. L. O. H. Rep., x, 1880 ; T. O. S., iii, 1883 ; Glaucoma, London, 1891.

FIG. 694.—APPARATUS FOR MEASURING THE VOLUME OF THE LENS.

Priestley Smith, T. O. S., iii. The graduated glass tube ends below in a bulb, B, closed by a perforated stopper, S. Above it terminates in a closed india-rubber tube, which can be compressed by means of the plate and nut, N. The volume of the lumen of the tube is 2·24 c.mm. per mm. ; the bulb and lower part of the tube are filled with rectified oil of turpentine. In taking a measurement the nut is screwed down until the fluid rises in the stopper to the transverse line. The height of the column in the graduated tube is then noted. The nut is then reversed until the fluid is drawn away from the stopper and bulb. The lens is then dropped into the bulb, the stopper replaced, and the fluid driven up to the mark. The volume of the lens is then read off on the scale.

As in the case of the cornea so for the lens, the maintenance of transparency and the conditions of optical refraction demand no expenditure of energy, and therefore involve no metabolic changes. The lens after death, and even after removal from the body, if placed in a suitable fluid, remains clear for a considerable time. The same considerations which account for the continued growth of the lens show that the older portions, forming the nucleus, must be regarded, even during life, as upon the border line of the living and the dead. Normal cuticular elements, after a certain period, are cast off from the surface. This is impossible in the case of the lens, yet these epithelial fibres retain their transparency unimpaired.

The absence of keratin is noteworthy, not only in the normal lens (*v. supra*) but also in the cataractous lens (Knies).
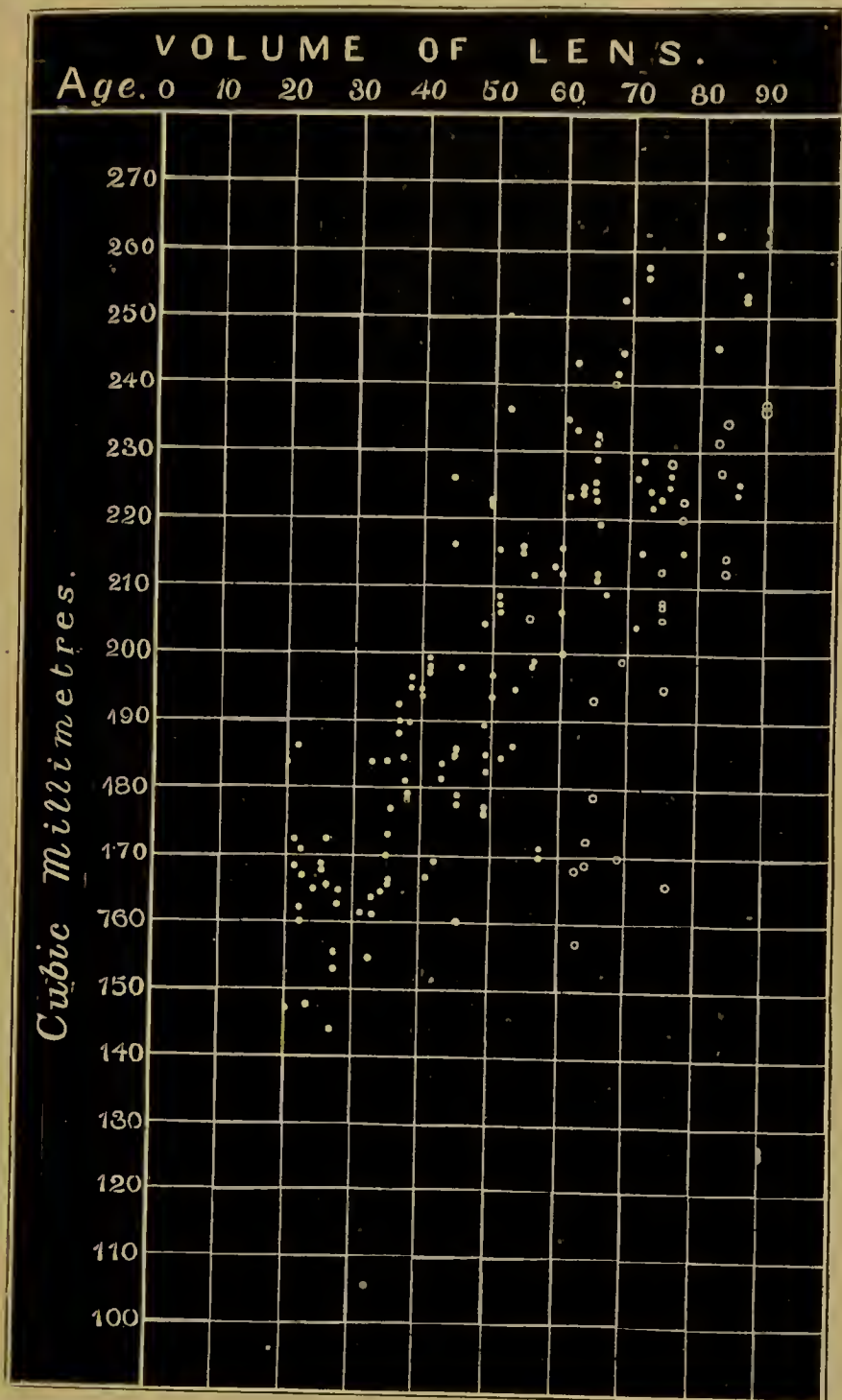
FIG. 695.—VOLUME OF THE LENS.

Priestley Smith, T. O. S., iii. The white dots show the transparent lenses, the circles partly or wholly cataractous lenses.

The lens is, however, extremely sensitive to changes in the character and concentration of the surrounding fluid. After death changes occur

in these fluids which eventually lead to clouding and opacity of the lens; these are dependent upon altered conditions of filtration and osmosis. Other influences, mechanical, physical, and pathological, lead to similar results, largely if not entirely due to the same agencies. It is therefore of prime importance to consider the properties and conditions of the lens and its constituent parts with reference to diffusion and filtration.

The chemical composition of the lens differs materially from that of the aqueous: it is therefore obvious that some protective influences are at work to prevent an approximation by osmotic and other physical processes. These are to be found in all probability in the capsule and its lining epithelium.

Fluid cannot enter the lens by filtration, since the capsule is under normal circumstances stretched; the internal pressure is therefore greater than the external. That the capsule is stretched is shown by the fact that the lens tends to assume the spherical form when it is freed from its surroundings. On the other hand, under some pathological circumstances, filtration of fluid outwards may occur, leading to loss of fluid and consequent shrinking.

Microscopical examination of the capsule with high powers fails to reveal any pores, and their absence is further proved by the results of filtration with colloid or finely granular dyes. Becker thought that the lens-fibres were separated by inter-fibrillary spaces: this has been disproved by Sernoff and Babuchin, and Henle's and Rabl's researches show that the fibres are in contact with the exception of a minimum of cement substance. There are therefore no preformed spaces in the lens, and, as in the cornea, interchange of fluid takes place by diffusion and not by actual flow.

Fig. 696.—Leber's Diffusion Apparatus.

The properties of the capsule with regard to diffusion and filtration can be investigated in the same manner as for Descemet's membrane. It is found that crystalloid substances diffuse rapidly through the capsule, as for example fluorescein, carmin, methyl violet, methylene blue, eosin, sodium chloride, potassium ferrocyanide, ferric chloride, silver nitrate, etc. (Meissner, J. Sinclair, Ulrich, van Geuns, Leber).

Soluble Berlin blue does not pass through either by diffusion or under a pressure of 150 mm. Hg.: indeed, this substance may be used as a control to show the absence of minute holes in the membrane. It also demonstrates the absence of preformed anatomical pores. The impenetrability to Berlin blue is not due to precipitation by salts contained in the membrane, since the same result is obtained if the membrane is previously soaked in distilled water. It appears that this substance has a great tendency to aggregation of its large molecules, so that they are too large to pass through the physical pores.

If the Berlin blue is deposited in the membrane itself by placing potassium ferrocyanide on one side and ferric chloride on the other, the membrane becomes deeply stained, and the stain cannot be removed by prolonged soaking in distilled water. Such a stained membrane is quite impermeable to either potassium ferrocyanide or ferric chloride.

The capsule is also impermeable to neutral litmus solution (Mays) and to Zsigmondi's colloidal gold solution. On the other hand, certain colloids, such as proteids and hæmoglobin, pass through, although their molecules are much larger than those of Berlin blue. v. Wittich first showed that albumin would filter through the capsule, and he wrongly stated that the percentage in the filtrate was equal to that in the original solution. van Geuns states that albumin will also diffuse, *i.e.* without pressure, and Leber has confirmed the observation with blood-serum, ascites fluid, and white of egg. He also filtered hæmoglobin through the capsule from ten times diluted blood, and clearly obtained the absorption bands of oxyhæmoglobin in the filtrate. Diffusion experiments with the uninjured lens show that proteids can pass in the reverse direction—*i. e.* out of the lens.

Filtration will take place under less than 10 mm. Hg pressure, but is slight even under high pressures. With 0·8 per cent. NaCl from 0·3 to 0·2 c.mm. per minute pass through under 30 mm. Hg, the amount gradually diminishing. The capsule is impermeable to oil and the fatty droplets in milk. Ulrich found the filtration through the posterior capsule four to seven times as great as through the anterior, easily explicable from its being so much thinner. It should be mentioned that van Geuns and Koster obtained different results with crystalloids, and deny the permeability of the lens capsule on filtration; their observations have been repeated and disproved by Leber.

Knies.—Untersuchungen aus d. physiol. Inst., Heidelberg, 1878. Sernoff.—Dissertation, 1867. Babuchin.—Stricker's Handbuch, ii, 1872. Henle.—Abhandl. d. k. Ges. d. Wissensch. zu Göttingen, xxiii, 1878. Rabl.—Z. f. wissensch. Zool., lxiii, lxv, lxvii, 1898, 1899. Meissner.—Z. f. rat. Med., xxxv, 1868. J. Sinclair.—Dissertation, Zürich, 1876. Ulrich.—A. f. A., xxxvi, 1898. van Geuns.—A. f. O., xlvii, 2, 1899. Leber.—B. d. o. G., 1899. Mays.—Verhandl. d. naturhist.-med. Ver. zu Heidelberg, iii, 1885. Zsigmondi.—Ann. d. Chemie, ccci, 1899. v. Wittich.—Virchow's Archiv, x, 1856. Koster.—A. f. O., li, 2, 1900.

Having considered the properties of the capsule, the osmotic conditions of the whole lens must now be investigated. Soluble diffusible substances pass into the lens and can be recognised by their chemical reactions when brought in contact with the lens after removal from the eye, or when injected into the vitreous, into the anterior chamber, under the conjunctiva, or into the circulation. They are absorbed extremely slowly, and long remain in the superficial layers alone. When injected into the circulation they enter the lens last of any part of the body, cartilage not excepted. Having entered, they remain here long after they have been excreted from the rest of the eye. These facts were first demonstrated in 1865 by Bence Jones : he administered lithium and other salts to animals, and determined the presence of the metals by spectrum analysis.

If a guinea-pig is fed with 0·18 grm. of lithium chloride it passes in

fifteen minutes into all the vascular parts of the body, into cartilage, and into the aqueous, but only after thirty to thirty-two minutes into the lens. After two and a half hours it is principally found in the cortex, after eight hours also in the nucleus, after twenty-six hours uniformly distributed. In three to four days lithium has disappeared from the evascular structures of the body, with the exception of the lens, in which traces may be found after thirty-three days. After subcutaneous injection lithium appears in the aqueous in four minutes, in the lens in ten minutes.

After administration of rubidium, cæsium, or thallium chloride, only traces could be found in the ash of the lens; after strontium chloride no trace even after eleven days with a total dose of 0·33 grm.

Administration of lithium carbonate shortly before death in man, or before cataract extraction, gave concordant results. The lithium was first found after two and a half to three hours in the lens, distributed throughout the lens in four to five hours; it had disappeared completely after seven days.

After intravenous injection of potassium ferrocyanide in dogs, Memorsky was unable to find the substance in the lens; Ovio failed to find it after subcutaneous injection in rabbits. On the other hand, Ulrich, after similar doses of 2—4 grms. subcutaneously in rabbits, found it in two hours in the equatorial part of the cortex, the posterior capsule remaining unstained. The same result was obtained with potassium iodide. Deutschmann found three hours after internal administration of potassium iodide in rabbits the strongest reaction in the posterior part of the cortex and at the equator.

Fluorescein acts similarly; the staining is confined to the peripheral cortex, and is much slighter after subcutaneous and intravenous injection than after direct injection into the vitreous (Schöler and Uhthoff, Panas, Ehrenthal, Ovio). Ulrich failed to find it at all in living animals.

The extreme slowness of diffusion into the lens is shown by direct injection into the vitreous. Knies found that after injection of 10 per cent. potassium ferrocyanide solution in rabbits it was only found after three or four hours, and then only in one sixth of the thickness of the lens. Weiss, under the same conditions, found it only in the posterior half, and only in considerable quantity in the outer layers. Ovio found it in the posterior layers and at the equator, and similarly with potassium iodide; only occasionally could it be found in the anterior cortex. After injection of 20 per cent. fluorescein into the vitreous, Ehrenthal found the coloration begin during the first day at the equator and spread thence to the posterior surface. Schöler and Uhthoff found the fluorescence of the lens under similar conditions commence only only after two to three days; it persisted, however, for weeks and even months, long after disappearance from the vitreous; the cortex cleared first, then the nucleus. Similar results are obtained by injection into the anterior chamber (Schöler and Uhthoff, Ehrenthal) or under the conjunctiva (Pflüger).

The slowness of diffusion is also shown by the results of placing the freshly removed lens in suitable solutions. It is important in

these experiments to choose solutions which are isotonic to the lens—
e.g. fluorescein in 1·2 per cent. NaCl, a mixture of 1·25 per cent.
potassium ferrocyanide with 1 per cent. NaCl, etc. (Leber). Ox lens
placed in this fluorescein solution for seven days shows only slight
staining of the periphery, the nucleus remaining unstained; even the
isolated nucleus shows only staining to the depth of 1½ mm. in two
days. Memorsky found that 1 per cent. potassium ferrocyanide pene-
trated throughout the lens in an hour and a half. Knies and Weiss
obtained staining of the cement substance with potassium ferrocyanide,
and Ulrich remarked that the fibres were unstained, whilst their nuclei
showed a blue edging. Leber obtained a peculiar staining of the
fibres after placing the lens in ferricyanide mixture and testing with
ferrous sulphate; they showed regularly arranged, deeply stained,
transverse stripes, fading off on each side, so that the greater part of
the fibres were unstained. Transverse sections showed that the staining
was almost confined to the surface of the fibres. A similar result may
be obtained by placing the lens in vitreous fluid coloured with methy-
lene blue.

Arnold transfused frogs for one to one and a half days with dilute
potassium ferrocyanide; on treating with ferric chloride blue colora-
tion was seen between the cubical cells and between the fibres. The
same occurred after prolonged transfusion with indigo-carmin if a
thread was passed through the anterior chamber, and the conjunctival
sac was irrigated with 1½ per cent. NaCl; also after introduction of
the dye into the anterior chamber.

From its osmotic properties the lens may be regarded simply as a
bladder filled with a saline albuminous solution. If the contents are
isotonic with the surrounding fluid no change occurs; a hypertonic
solution abstracts water from the lens, causing loss of weight and
shrinking; a hypotonic solution gives up water to the lens, causing
increase of weight and swelling. This is true only in a broad sense,
since there is evidence that the capsule and its epithelium play a
regulating part, at any rate *intra vitam*.

Deutschmann found that the lens immersed in 20 per cent. to
between 2 and 1 per cent. NaCl lost weight, whilst it gained in solu-
tions of less concentration: in both cases a superficial haziness was
noticed. If the lens was laid in water fluid accumulated under the
capsule and strongly refracting droplets were pressed out of the fibres.
The cause of the swelling is the large percentage of proteid in the lens,
amounting to 35—37 per cent., varying in different animals. The
human lens is particularly sensitive to changes in the surrounding
fluid, and the fibres show an unusually great tendency to swell. Even
isolated lens nuclei take up 84 per cent. of their weight of distilled water
in twenty-four hours (Jäger).

In concentrated NaCl solutions the preliminary diminution in
weight is followed by an increase, which is, however, much less than in
hypotonic solutions. It is due to the fact that after the saline con-
stituents have become equalised the excess of proteid in the lens causes
absorption of water; this is proved by placing the lens in serum con-
taining a large amount of NaCl, when the second phase does not occur.

Manca and Ovio determined for ox and frog lenses the concentrations of various salts which were isotonic—*i. e.* those in which the lens neither gained nor lost weight, also those in which they did not become hazy ; the results were identical. For the ox lens 1·2 per cent. NaCl is isotonic, for the frog's 0·8 per cent. Other crystalloids—*e. g.*, potassium or lithium chloride, glucose, etc.—the concentration varies with the molecular weight, and can be calculated from the osmotic coefficient of the lens. Thus the coefficient for the ox lens is 0·0205, so that for NaCl the percentage is 58·5 × 0·0205 = 1·2 per cent.; for LiCl, 42·5 × 0·0205 = 0·87 per cent.

The lens is found to act exactly like the red corpuscles : thus in the ox isotonic solutions for the lens = 1·2 per cent., for the red corpuscles = 0·9 per cent. ; in the frog, for the lens = 0·8 per cent., for the red corpuscles = 0·6 per cent. : *i. e.* 1·2 : 0·9 = 0·8 : 0·6.

In the living body the conditions are different, since the lens remains clear and unaltered in weight, although the surrounding fluids are by no means isotonic. The osmotic equivalent of ox aqueous is 0·96—0·99 per cent. NaCl (Kunst, Manca and Deganello), whereas 1·2 per cent. NaCl is isotonic for the lens. The osmotic equivalent of the vitreous is the same as that of the aqueous (Kunst). The ox lens placed in aqueous or vitreous gains 0·085—0·1 per cent. of its weight per hour for the first fifteen hours (Leber) ; it remains clear. The rabbit's lens gains 0·57 per cent. per hour in aqueous and becomes opaque. The human lens gains in weight and thickness after death, as may be proved by repeated determinations, the lens being replaced in the eye in the intervals (Jäger and Kletzinsky). The specific gravity and solids of the aqueous increase, so that in forty-eight hours they are almost doubled, the solids consisting principally of proteids, which increase from 0·05 to 0·58 per cent. The salts also increase absolutely, though they diminish relatively to the total weight of dried solids. The changes are the same as occur on placing the lens in hypotonic solutions, and clouding similarly takes place—in man commencing in six to eight hours, in the pig and calf only in eighteen to twenty-four hours (Düsing).

The lens during life therefore differs in its behaviour from the dead lens in retaining a constant amount of water and in retaining its proteid whilst immersed in a fluid which is not isotonic with it. The *post-mortem* interchange may, however, occur within the living body when the lens is dying or dead, as for example in cataract, and this accounts for the stages in the ripening of cataract. During the first stage water enters the lens (Deutschmann) and proteid is given out to the aqueous (*v.* Jäger, Leber, Deutschmann). During the second stage the increased tension of the capsule causes albuminous fluid to filter out, so that the volume of the lens gradually diminishes. The first stage is therefore due to osmosis, the second to filtration.

Bence Jones.—Proc. Roy. Soc., xiv, 1865. Memorsky.—A. f. O., xi, 2, 1865. Ovio.—Ann. d'Oc., cxxiv, 1900. Ulrich.—A. f. O., xxvi, 3, 1880. Ottolenghi.—Ann. di Ott., xv, 1886. Schöler and Uhthoff.—Jahresberichte ü. d. Wirksamkeit d. Augenklinik f. 1881. Panas.—A. d'O., vii, 1887. Ehrenthal.—Dissertation, Königsberg, 1887. Ulrich.—A. f. A., xii, 1883. Knies.—Virchow's Archiv, lxv, 1875. Weiss.—Verhandl. d. natur-hist.-med. Ver. zu Heidelberg, ii, 1877. Pflüger.—Soc. franç. d'O., 1891. Arnold.—

Virchow's Archiv, lxvi, 1876. LEBER.—In G.-S., 1903. DEUTSCHMANN.—A. f. O., xxiii, 3, 1877; xxv, 2, 1879. JÄGER —Ueber die Einstellungen des dioptrischen Apparates, Wien, 1861. MANCA AND OVIO.—Arch. di Ott., xxvii, 1898. KUNST.—Dissertation, Freiburg, 1895. MANCA AND DEGANELLO.—Arch. di Ott., xxvii, 1898. DÜSING.—Das Krystalllinsen-system des menschlichen Auges, Berlin, 1844.

The *intra vitam* protective mechanism against osmotic changes must lie in the capsule and its epithelium, as long ago pointed out by Leber. The importance of the cubical epithelium is exemplified by many pathological and experimental observations. After removal from the eye the epithelium quickly undergoes *post-mortem* changes, and degenerative changes occur after massage of the lens, as the result of disordered circulation in the choroid and ciliary body, after administration of naphthalin, etc.; all these causes lead to opacification, which is in some degree, if not entirely, explicable upon physical grounds. Similarly there are rare cases of spontaneous absorption of senile cataract, and here complete absence of the capsular epithelium has been observed (Mitvalsky, E. v. Hippel).

Deutschmann considers that some experiments which he devised disprove the protective action of the epithelium. He bisected an eye equatorially, removed the vitreous and posterior lens capsule, carefully removed the lens, brushed the epithelium off the back of the anterior capsule, and then replaced the lens. After twenty-four hours or more in man and in various animals the lens remained clear. In other experiments the capsule was tied on a tube filled with 0·75 per cent. NaCl and the lens placed upon the capsule; it remained clear whether the epithelium was removed or not. On the other hand, it rapidly became cloudy if it was placed directly in 0·75 per cent. NaCl, or aqueous after removal from the capsule. Deutschmann concludes that the epithelium has no protective influence, but all that is really proved is that the time was not sufficient to demonstrate this influence, and that the capsule itself probably affords some protection.

Much more difficult to explain is the retention of transparency when the lens is dislocated into the vitreous, since the posterior capsule has no epithelial lining. Barabaschew has shown that the lens-fibres over the whole posterior surface have broad ends which are applied, like mosaic, to the capsule; it is possible that this arrangement acts in the same manner as the cubical epithelium.

The mode of distribution of the nutrient fluids through the lens during life is almost entirely a matter of conjecture. Many foreign substances pass between the epithelial cells and between the lens-fibres, whilst others, like fluorescein, seem to permeate the fibres themselves. Erroneous deductions have been made from the results of retention of a particle of steel within the eye. Brown spots may then be seen to accumulate in the anterior layers of the lens, forming a circle corresponding with the edge of the dilated pupil. Samelsohn concluded that fine particles of rust were formed from the foreign body within the lens, and were carried by a stream to pores in the capsule, where they were retained. The circle may, however, be observed not only with foreign bodies in the lens but also in the vitreous, and the particles are not free, but are contained in proliferated capsular epithelial cells. The true explanation is that the iron is dissolved slowly by the carbon

dioxide in the lymph, forming a diffusible solution, which is carried into the lens and elsewhere, and is deposited as an insoluble compound in the tissues (Leber). The affinity of the cells and other tissue elements for iron, which probably forms an albuminate, is shown by the investigations of E. v. Hippel and others on siderosis bulbi. The iron is especially deposited in the retinal pigment epithelium and in the epithelium of the lens capsule. The distribution of the metal is by diffusion, and there is no question of fluid streams : the formation of a ring corresponding with the pupillary margin is not yet explained.

MITVALSKY.—C. f. A., xvi; 1892. E. v. HIPPEL.—B. d. o. G., 1893. DEUTSCHMANN.—A. f. O., xxiii, 3, 1877. BARABASCHEW.—A. f. O., xxxviii, 3, 1892. SAMELSOHN.—K. M. f. A., xix, 1881. LEBER.—Internat. Med. Congress, London, 1881. LANDMANN.—A. f. O., xxviii, 2, 1882. E. v. HIPPEL.—A. f. O. xl, 1, 1894.

The effects of giving the aqueous access to the lens-fibres is seen in the operation of discission. Simple opening of the capsule, without injury to the lens-fibres, suffices to cause swelling and opacification ; deep needling increases the effect only by aiding the entrance of aqueous and bringing it into contact with more fibres. The lenses of different animals vary much in their reaction. In the frog even deep injury leads only to partial and transient opacity (P. Knapp). In the rabbit the opacity is usually localised. This is largely due to early and free deposition of a protecting network of fibrin, under which the epithelium proliferates and forms a capsular scar. New fibres are laid down under the capsule, so that the opaque area is gradually pushed farther from the surface (cf. Vol. II, p. 413).

In man the lens shows very marked tendency to swell and become opaque ; partial opacity is very rare, and restoration of transparency, apart from absorption, scarcely ever occurs, though it cannot be absolutely denied, especially for the posterior cortex. The extreme susceptibility of the human lens is probably due to the watery nature of the aqueous as compared with that of other animals. The results of injury of the posterior capsule are much slighter ; the opacity remains localised, though the swollen lens material projects into the vitreous (Boë).

Histologically the effect of needling is first to cause the formation and expression of highly refractile droplets from the cortical fibres anterior to the nucleus, and secondly the development of clefts between the fibres of the posterior cortex rather anterior to the capsule and around the nucleus (Schlösser). The clefts are caused by increase in the length of the cortical fibres, the denser nuclear fibres remaining less affected ; hence the outer fibres tend to become folded. The further microscopical changes which occur are those already described for cataract in general (v. Vol. II, p. 392).

Similar changes occur without opening the capsule after massage of the lens with a blunt instrument introduced into the anterior chamber (Schirmer, Hess). The extent and duration of the opacity depend upon the force and duration of the massage. The operation injures the epithelium, so that abnormal diffusion through the capsule is permitted (Schirmer) ; hence the similarity of the changes to those of discission. The distortion and destruction of epithelium under the

anterior capsule after even gentle massage are brought out well by staining with methylene blue dissolved in 0·75 per cent. NaCl; the epithelium and the parts of the cortex which are unprotected by epithelium stain deep blue and retain the dye.

P. KNAPP.—Z. f. A., iii, 1900. BOË.—A. d'O., vi, 1886; vii, 1887. SCHLÖSSER.— Experimentelle Studien ü. traumatische Kataract, München, 1887. HESS.—B. d. o. G., 1887. SCHIRMER.—Dissertation, Greifswald, 1887; A. f. O., xxxiv, 1, 1888. DEMARIA.—A. f. O., lix, 3, 1904.

The effects of the abstraction of water upon the lens require more detailed consideration on account of their relationship to diabetic cataract. If 0·2 grm. of sodium chloride is injected subcutaneously, or placed in the stomach of a frog, besides great loss of water from the skin, the lens becomes opaque, the anterior chamber becomes very deep, and the corneal curvature is increased (Kunde). If the frog is placed in water death is averted, and the lens regains its transparency; if the dose is smaller the lens may clear without the external application of water. Other crystalloids, such as sodium nitrate, large quantities of cane-, grape-, or milk-sugar, act in the same manner (Kunde, Richardson, Heubel). In mammals it is much more difficult to produce the opacity. It is easiest in kittens, 1—2 grms. NaCl being introduced into the stomach or rectum. Rabbits generally die before the lens becomes cloudy, but Richardson succeeded with 60 grm. of syrup introduced into the peritoneal cavity. Heubel succeeded with cats and dogs by intravenous injection of sodium chloride or sulphate; with lethal doses he observed the cataract develop after the death of the animal. In cats the opacity commences at the equator, and is limited to the superficial layers; Deutschmann found the same in frogs, but Kunde states that this is not constant and that the deeper layers are also affected. The opacity disappears if the lens is removed and placed in water.

Kunde considered that the phenomenon is due to abstraction of water, since it occurs with 2 per cent. NaCl and also on freezing. Michell opposed this explanation on the grounds that the lens does not become opaque on drying, nor does it in frogs when they are kept at a high temperature under a bell-jar. Guttmann did not obtain clouding with sodium sulphate or potassium salts, nor with calcium chloride. It is, however, only a question of time. Frogs placed in an atmosphere dried by calcium chloride develop cataract and die in one day, whereas without calcium chloride they live five or six days, and do not develop cataract (Köhnhorn, Deutschmann). Sodium sulphate also gives a positive result if the high molecular weight is taken into account and a correspondingly high dose is given (Heubel). Potassium chloride in small doses is too quickly excreted, and in large doses it kills the animal by its action upon the heart.

Deutschmann injected 10 per cent. NaCl into the anterior chamber, and found that in rabbits and dogs the anterior surface of the lens became opaque over an area limited to that exposed by the pupil; it cleared up in a few days or weeks. Heubel obtained cataractous changes in frogs and mammals by introducing powdered salts mixed with a minimum of water into the conjunctival sac; the lens became

milky-white in ten to fifteen minutes, the cornea remaining clear until the next day, when the lens was again transparent. The kerato-conjunctivitis is very intense in warm-blooded animals, going on to ulceration, whilst the lenticular opacity is very transient. Almost any crystalloid will produce the result, varying in rapidity and degree according to the hygroscopic effect. By weighing one lens of the frog before and the other after the experiment Heubel found that there was a loss of water of 2—5·5 per cent.

Loss of water alone is not a sufficient explanation of the opacification, since the lens remains clear on drying or on placing in glycerine, etc. (v. Michel). Kunde conjectures that the entry of salts, Heubel that the abstraction of water, leads to other, as yet unexplained, changes in the lens. Heubel made the interesting observation that if sodium chloride is injected under the skin of a frog, and one anterior chamber is evacuated, then only the lens of the opposite side becomes cloudy. Further, if so much salt is administered that the animal becomes moribund the lens remains clear; on placing the frog in water circulation is restored and the lens becomes opaque. It is clear, therefore, that the condition is not due to the general effects of the salts upon the body, but solely to the concentration of the aqueous. Loss of water from the whole body may be very marked, as, for example, in cholera, without the lens becoming opaque.

A remarkable observation was made by J. R. Ewald, that the opacity induced by abstraction of water is removed by massage of the lens or by shaking. In guinea-pigs, rabbits, cats, dogs, etc., the lens becomes opaque in the pupillary area ten to twenty hours after death, unless precautions against drying are taken. Massage through the cornea, or a sharp blow upon the head with a wooden mallet, causes the opacity to clear up. Leber has shown that the opacity produced by Heubel's method also clears up with light massage. It is probable that the mechanical interference causes water to be absorbed from the subcapsular layer which accumulates after death, so that the lens-fibres swell and regain their normal refractive index (Leber).

It has already been pointed out that diabetic cataract cannot be explained upon the old theory of the abstraction of water owing to the presence of sugar in the aqueous (v. Vol. II, p. 426). Deutschmann has shown that a 5 per cent. solution of sugar is necessary to produce opacity, whilst in a diabetic patient with 8 per cent. sugar in the urine not more than 0·5 per cent. sugar is found in the aqueous. Heubel has strongly supported the hygroscopic theory, stating that a 0·75 per cent. NaCl solution causes opacity in the human lens, whilst a 0·6 per cent. NaCl solution to which 1 per cent. sugar is added leaves the lens clear. The explanation, however, is obvious, as pointed out by Deutschmann. The latter solution is isotonic to a 0·92 per cent. NaCl solution, which is isotonic to the lens, therefore no clouding occurs; 0·75 per cent. NaCl on the other hand, is hypotonic to the lens. It is practically impossible to produce lenticular opacity by injecting sugar, except in frogs. Deutschmann succeeded in raising the sugar content of the aqueous to only 0·2 per cent. and of the vitreous to 0·3 per cent. in rabbits by tying the renal vessels. Moreover, there is swelling of the

lens, as opposed to shrinking, in diabetic cataract. The lens also contains sugar in some diabetic cataracts, and under these circumstances its hygroscopic effect is abolished. Thus in the glycosuria following extirpation of the pancreas in dogs, Cavazzani found the clear lens to contain sugar in the peripheral layers; with 10 per cent. in the urine there was only 0·3 per cent. in the aqueous.

KUNDE.—Z. f. wissensch. Zool., viii, 1857. RICHARDSON.—Med. Times and Gaz., 1860. HEUBEL.—Pflüger's Archiv, xx, 1879. DEUTSCHMANN.—A. f. O., xxiii. 3, 1877. MITCHELL. —Amer. Jl. of Med. Sc., xxxix, 1860. GUTTMANN.—Berliner klin. Woch., 1865. KÖHNHORN. —Dissertation, Gryph., 1858. v. MICHEL.—Festschrift, Würzburg, 1882. J. R. EWALD.— Pflüger's Archiv, lxxii, 1898. DEUTSCHMANN.—Pflüger's Archiv, xx, 1879; xxii, 1880. HEUBEL.—Pflüger's Archiv, xxi, 1880. CAVAZZANI.—Ann. di Ott., xxi, 1892.

If a frog is frozen the lens becomes opaque before the animal dies, the opacity disappearing on thawing (Kunde). The opacity is limited to the cortex (Abelsdorff). The frog may be reduced to a temperature of −12° C. without killing it; on gradually thawing the lens clears up, but again becomes hazy when the animal begins to move. The primary opacification passes off in about half an hour; the latter may assume the form of a capsular cataract, and may be accompanied by opacification of the cornea; even if both disappear the eye may remain blind (de Crecchio). Microscopically there are the same vacuoles as after immersion in saline solutions, and the cause is probably the abstraction of water (Kunde). If the human lens is frozen it becomes completely opaque, and on thawing clears up from the periphery, the posterior pole clearing last (v. Michel). Leber found that the opacity in the frozen calf's lens was simply due to increased refractive index of the frozen lens-fibres.

In many new-born or very young animals cooling to nearly 0° C. causes opacification of the lens, which disappears at a slightly higher temperature. It is limited to the nucleus, and is most easily observed in calf's lenses and in new-born cats. It was attributed by Henle to the formation of fatty vacuoles, but this view is not supported by their behaviour with osmic acid or other fat stains (Daddi). There is no doubt, however, that the opacity on cooling differs in some essential characteristics from that on freezing. It disappears even at the low temperature on placing the lens in glycerine.

The lens becomes opaque on heating to 80° C. owing to coagulation of the proteids, and this opacity of course is permanent (v. Michel). The temperature may be slowly raised to 65° C. without causing complete opacity (Daddi). Crystallin α, coagulating at 72° C., is predominant in the cortex, crystallin β, coagulating at 63° C., in the nucleus (Mörner).

The causation of cataract in glass-blowers is interesting in this connection (Meyhöfer—11·6 per cent. in 506 glass-blowers, Röhlinger— 7·6 per cent. in 287, Robinson). It cannot be due to the mere raising of the temperature of the lens, since the aqueous is a bad conductor of the dark heat rays, and the temperature could not be raised to the requisite extent without burning the cornea: molten metal may, indeed, cool between the lids and the globe without producing cataract. The cause is probably to be found in the enormous increase of evaporation

from the surface of the cornea, aided by the continual sweating from the skin (Leber).

KUNDE.—A. f. O. iii, 2, 1857. ABELSDORFF.—C. f. Physiol., 1899. DE CRECCHIO.—Il Morgagni, 1866. V. MICHEL.—In Leber, G.-S., 1903. HENLE.—Abhandl. d. k. Ges. d. Wissensch. zu Göttingen, xxiii, 1878. DADDI.—Ann. di Ott., xxvii, 1898. MÖRNER.—Z. f. physiol. Chemie, xviii, 1893. MEYHÖFER.—K. M. f. A., xxiv, 1886. RÖHLINGER.—Dissertation, München, 1888. ROBINSON.—Brit. Med. Jl., 1903.

Light rays and chemically active ultra-violet rays have no action on the lens except after prolonged application in extraordinary concentration : ultra-violet rays are indeed absorbed by the lens (Widmark, Schulek, Hertel, Birch-Hirschfeld), which thus acts as a protective mechanism for the lens. Czerny observed lenticular opacity in the rabbit and toad follow short application of direct sunlight concentrated by a convex lens. Werneck and M. Langenbeck obtained similar results. Widmark caused slight opacity in the rabbit by prolonged action of concentrated light from an arc lamp ; he attributed it to the ultra-violet rays. Action for two to four hours from a 1200-candle-power lamp in the atropinised eye was necessary, and even then only succeeded in four out of eleven cases. Ogneff failed to obtain any change on brief application from a 5000—6000 candle-power lamp.

WERNECK.—v. Ammon's Z. f. O., iv, 1834. LANGENBECK (1859).—In Leber, G.-S., ii, 2, 1903. CZERNY.—Sitz. d. k. Akad. d. Wissensch., lvi, 1867. WIDMARK.—Skand. Archiv, i, 1889 ; iii, 1892 ; iv, 1893. SCHULEK.—Ungar. Beitr. z. A., i, 1895 ; ii, 1896. SCHWITZER.—Ungar. Beitr. z. A., ii, 1896. OGNEFF.—Arch. f. Physiol., 1896. HERTEL.—B. d. o. G., 1903. HERZOG.—B. d. o. G., 1903. STREBEL AND v. AMMON.—Deutsche med. Woch., 1903 ; K. M. f. A., xlii, 1903. *BIRCH-HIRSCHFELD.—B. d. o. G., 1903 ; A. f. O., lviii, 3, 1904 (Bibliography).

Lightning cataract, apart from the observations already made, might be considered to be due to the great richness of the electric spark in ultra-violet rays, but electrolytic and mechanical changes in the eye must not be forgotten. The effects of lightning on the eye differ from ophthalmia electrica in that cataract does not occur in the latter condition (*cf.* Terrien). In the former there is probably a direct action upon the ciliary body and lens epithelium. Thus, both Hess and Kiribuchi found changes in the capsular epithelium in their experiments. The causation of lightning cataract has received a variety of explanations. Leber attributed it to coagulation of the lens substance due to katalytic action, though he has since rejected this view : Silex to albuminous coagulation due to temperature. Vossius appeals to the iridocyclitic changes and Peters to the concentration of salts in the aqueous.

LEBER.—A. f. O., xxviii, 4, 1882. PAGENSTECHER.—A. f. A., xiii, 1884. LAKER.—A. f. A., xiv, 1885 ; in G.-S.. ii, 2, 1903. KNIES.—A. f. O., xxxii, 3, 1886. SILEX.—A. f. A., xviii, 1888. HESS.—Seventh International Congress, 1889. BULLER.—A. f. A., xxi, 1890. VOSSIUS.—B. z. A., iv, 1892. PREINDLSBERGER.—Wiener klin. Woch., 1900. PETERS.—B. d. o. G., 1900. KIRIBUCHI.—A. f. O., l, 1, 1900. TERRIEN.—A. d'O., xxii, 1902. BIRCH-HIRSCHFELD.—A. f. O., lviii, 3, 1904.

Interference with the ciliary circulation leads to opacification of the lens. In section of the posterior ciliary arteries it is the posterior long ciliaries which play the most important part (Wagenmann). Similar

results follow widespread embolism of the ciliary vessels (Herrnheiser), and extirpation of the iris and ciliary body in rabbits (Deutschmann). The characteristic change after section of the long posterior ciliary arteries is acute necrosis of the lens, shown by vacuolation and separation of the capsular epithelium and defective staining of the nuclei. The posterior cortex is separated from the capsule by a layer of albuminous material; the lens-fibres are softened, and break up. Finally, the lens shrinks, whilst proliferation of the capsule-cells leads to the formation of capsular cataract and irregular fibres.

Similar, though less extensive, changes follow ligature of the venæ vorticosæ (Koster Gzn, van Geuns). Striæ in the lens may be seen as early as ten hours after the operation (E. v. Hippel), and total cataract may occur in seven days (van Geuns). The development of cataract is, however, by no means constant, and appears to depend upon adequate interference with the circulation, amounting to almost complete cessation. Doubtless the associated increased tension is an important factor. The changes are probably due to primary epithelial necrosis (van Geuns), but the diminished vitality is partial and incomplete, since the opacity is often long delayed—even to weeks or months —and a considerable degree of regeneration occurs.

WAGENMANN —A. f. O., xxxvi, 4, 1890. HERRNHEISER.—Lotos, 1902. DEUTSCHMANN. —A. f. O., xxvi, 3, 1880. KOSTER GZN.—A. f. O., xli, 2, 1895. VAN GEUNS.—A. f. O., xlvii, 2, 1899. E. v. HIPPEL.—In Leber, G.-S., 1903.

The question of *the causation of senile cataract* is a difficult one which has not yet received a satisfactory answer. It may be most conveniently treated here, since it is intimately related to the nutrition of the lens. The earlier theories may be passed over as only of historical interest (*see* Magnus). So, too, persistent vascularisation of the lens-capsule, etc. (v. Walther, Düsing), need not be seriously discussed. The chief theories may be grouped into three classes : (1) in which the cause is to be found within the lens itself; (2) a chemico-physical theory, the nutrition of the lens suffering from the nature of the pabulum supplied to it by the ciliary body ; (3) in which the cause is to be discovered in some general disease or dyscrasia.

The principal theory of the first class was put forward by O. Becker, and is supported by Deutschmann ; the ætiological moment is here found in an unequal sclerosis of the older lens fibres. If the sclerosis of the nucleus does not progress uniformly stress and strain will be exerted upon the cortical fibres, and this will manifest itself first at the equator. The theory demands highly problematical postulates, and in any case affords no true solution to the question, since the cause of the irregular sclerosis is not explained. Schön found the cause in strong accommodative efforts, whereby the capsule is thrown into small folds; this leads to proliferation of epithelium near the insertion of the middle fibres of the suspensory ligament behind the equator, and near the insertion of the anterior fibres in front of the equator. It is doubtful whether the cause would produce the described effect, and in any case senile cataract is not more common in hypermetropia, as would be expected (Hess). Magnus considers that the sclerosis of the nucleus

impedes the flow of nutrient fluid, so that, as in naphthalin and other forms of cataract, three zones of opacity arise, an anterior and a posterior near the equator, and later one at the posterior pole. Mörner thinks that the progressive loss of soluble proteids may stop the transmission of light.

The chemico-physical theory has been warmly advocated by Peters in a series of papers; it applies to various forms of cataract as well as senile, and predicates a shrinking of the nucleus, brought about by interference with the normal supply of nutriment. Cases had previously been reported of cataract occurring in association with tetany or convulsions (Logetschnikow, Saemisch, Wettendörfer). Peters considers that cramp of the ciliary muscle occurs and causes irregularity in the supply of lymph. He describes changes in the epithelium of the ciliary processes, but these differ little if at all from those described by Kuhnt and Kerschbaumer as senile changes (v. Vol. I, p. 357). The details of this theory must be sought in the original papers of Peters and in the adverse criticism by Leber.

It was only natural that the cause of senile cataract should be sought in some general dyscrasia or disease, especially when it is remembered that the condition is bilateral. Most of the suggestions are unsupported by any satisfactory evidence. Thus, v. Michel's theory invoking sclerosis of the carotid arteries may be dismissed as disproved (v. Karwat, van Brömmel, Nickelsburg). Similarly, Deutschmann and Grilli's association of senile cataract with nephritis does not survive critical statistics (Schlesinger, Rotziegel, Ewetzki, Funke). The prevalence of brilliant sunlight and heat in India has been considered the cause of the frequency of cataract there. Careful investigation has failed to reveal any case of cataract due to light or ultra-violet rays (Schulek, Schwitzer, Widmark, Herzog, Birch-Hirschfield) (v. p. 1020). Heterochromia as an ætiological factor in cataract (Hutchinson, Malgat, Bistis, Schapringer, Weill, Fuchs) may be considered disproved; the apparent association is really one of complicated cataract with irido-cyclitis, the heterochromia being due to the latter cause. Vossius has drawn attention to the association of cataract with myxœdema (Landsberg, Hoffmann, Schiller, Westphal, Vossius, Becker); the occurrence of tetanic spasms in cases in which the thyroid is not functionally active is interesting in this connection. It is by no means improbable that auto-intoxication may play a part in the causation of senile cataract (cf. Hess). Römer's hypothesis, attributing senile cataract to the action of cytotoxins, will be considered elsewhere (v. infra).

Most authors have observed the influence of *heredity* in causing cataract. The subject has recently been investigated by Nettleship, who has collected a remarkable series of cases. He divides acquired or post-natal cataract into two groups—senile, occurring after, and presenile, or juvenile, occurring before forty years of age. It is found that when cataract, acquired at whatever age, occurs in more than one generation, it descends in the great majority of cases from parent to child, seldom skipping a generation, but that it is not uncommon for collaterals to be also affected. In childships (*i.e.* consisting of siblings or children of one parentage) of acquired cataract it is usual for the

affected siblings to occur in succession—*i. e.* not separated by unaffected children. When several siblings in succession suffer from acquired cataract, the liability to cataract will be found to have run through several generations, or to have been intensified by inheritance from both parents. Hereditary acquired cataract appears to descend more frequently through the mother than the father; this may be vitiated by paucity of data, difficulty in obtaining family histories of men, or woman's greater expectancy of life. In certain stocks of acquired cataract the disease has a special tendency to select one sex to the exclusion of the other, though it is doubtful whether either sex has a marked preponderance to this tendency. There seems to be a slight tendency for hereditary acquired cataract to occur earlier, or at least to ripen earlier, in each succeeding generation, but it is not uncommon to find that the cataract has come on at about the same age in all the affected members of a family (Bowman). In many such cases the age is comparatively early (Fuchs). Certain cases raise the question whether such anticipation may not be carried so far as to reach the child *in utero* and thus lead to some form of congenital cataract.

In congenital cataracts, those with complete opacity from birth, or soon after, are probably due to some general morbid condition often powerfully affecting the whole offspring and sometimes occurring in both parents : there is no mention of syphilis. Fusiform, axial, spindle (Knies, Leber), or coralliform (Marcus Gunn) cataract commence very early in life and are almost stationary; they show some features in common with lamellar cataract. They appear to be frequently hereditary (*v.* p. 806). Transmission is continuous, attacking successively born siblings often, but by no means always. The first-born, whether boy or girl, is usually affected. Of forty-six cases, twenty-five were male, twenty-one female. Nettleship gives one extraordinary pedigree of five generations containing more than ninety persons, thirty of whom are known to have had cataract (Fig. 567). From the history, the cataract must have been present at birth in all cases. Lamellar cataract usually affects only one member of a family or stock, but exceptions are not very rare. Nettleship reports nineteen families. In ten families, where two or more generations suffered, descent was continuous in all. Descent was through the mother in thirteen generations, through the father in six; it was to the same sex in thirteen generations, to the opposite sex in eight.

Magnus.—Geschichte des grauen Stares, Leipzig, 1876. von Walther.—Ueber d. Krankheiten d. Krystalllinse, Landshut, 1810. Düsing.— Das Krystalllinsensystem d. menschlichen Auges, Berlin, 1844. O. Becker.—In G.-S., v, 1877. Deutschmann.— A. f. O., xxv, 1, 1879. Schön.—A. f. O., xxxiii, 1, 1887. *Hess.—In G.-S., 1905. Magnus. —A. f. O., xxxvi, 4, 1890. Mörner.—Z. f. physiol. Chemie, xviii, 1893. Logetschnikow.— K. M. f. A., x, 1872; Moskauer ophth. Ges., 1900. Saemisch.—See Hess. Wettendörfer. —Wiener med. Woch., 1897; B. z. A., xxxviii, 1899. Peters.—A. f. O., xxxix, 1, 1893; xl, 3, 1894; Z. f. A., v, 1901; K. M. f. A., xxxix, 1901; B. d. o. G., 1901–1903; K. M. f. A., lxii, 1904. v. Michel.—Horner's Festschrift, Wiesbaden, 1881; Lehrbuch, 1884. v. Karwat. —Dissertation, Würzburg, 1883. van Brömmel.—Dissert., Würzburg, 1886. Nickelsburg. —Dissert., Würzburg, 1892. Deutschmann.—A. f. O., xxix, 3, 1883. Frenkel —A. d'O., xviii, 1898. Grilli.—Soc. franç. d'O., 1904. Schlesinger.—Dissertation, Berlin, 1884. Rotziegel.—Allg. Wiener med. Ztg., 1886. Ewetzki.—A. d'O., vii, 1887. Funke.— Dissertation, Berlin, 1896. Schulek.—Ungar. Beiträge z. A., ii, 1900. Schwitzer.—See Hess. Widmark.—Skand. Archiv f. Phys., i, 1889; iii, 1891; Beiträge z. Ophth., Leipzig

1891; Mitteilungen der Augenklinik zu Stockholm, 1898, 1901. *BIRCH-HIRSCHFELD.— A. f. O., lviii, 3, 1904. HUTCHINSON.—R. L. O. H. Rep., vi, 1, 1867; 4, 1869. MALGAT.— Rec. d'O., 1895. BISTIS.—C. f. A., xxii, 1898. WEILL.—Z. f. A., xi, 1904. *FUCHS.— Z. f. A., xv, 1906. LANDSBERG.—C. f. A., xii, 1888. HOFFMANN.—Deutsche Z. f. Nerven-heilk., 1896. SCHILLER.—Beiträge z. klin. Chir., xxiv, 1899. WESTPHAL.—Berliner klin. Woch., 1901. VOSSIUS.—B. d. o. G., 1902; Z. f. klin. Med., 1905. BECKER.—Dissertation, Giessen, 1902. KLAMROTH.—Dissertation, Greifswald, 1874. APPENZELLER.—Dissertation, Tübingen, 1884. HIRSCHBERG, PURTSCHER, SCHANZ.—C. f. A., xxi, 1897. HOSCH.— Hagenbach-Burckhardt's Festschrift, 1897. WESTHOFF.—Ann. d'Oc., cxix, 1898. DAUST. —Dissertation, Kiel, 1899. HOROVITZ.—Dissertation, Berlin, 1903. HUNTER.—Lancet, 1905. *NETTLESHIP.—R. L. O. H. Rep., xvi, 3, 1905.

THE CONJUNCTIVA

The distribution of the conjunctival and subconjunctival or epi-scleral vessels has already been described. The actual circulation in these vessels and in new-formed corneal vessels can be observed micro-scopically during life (Coccius, Donders, Balser, Preiss, Friedenwald, Sergejew, Bajardi, Schleich, Augstein).

Absorption from the conjunctiva is less impeded by the epithelium than from the cornea owing to the rapid blood and lymph flow. It is, however, comparatively slight on account of the small surface, and it is practically impossible to cause the absorption of lethal doses if care is taken to obstruct temporarily the lacrymal sac. Atropin, silver nitrate (v. Vol. I, p. 110), calomel (Kämmerer, Alsberg), etc., have been the chief objects of experiment. The absorption of finely-divided solids, e.g. Indian ink, is effected by means of leucocytes (Leber). Micro-organisms are unable to effect an entrance and produce general infection if the epithelium is intact and if the lacrymal passages are obstructed. If the latter precaution is not taken, infection may occur (Römer, Mayer, Stock).

More interesting at the present time are the effects of subconjunc-tival injections. It has been shown that fluorescein (Pflüger) and potassium iodide or ferrocyanide of iron (Addario, Wessely) pass in appreciable quantities into the interior of the eye by this route. Soluble mercury salts, on the other hand, cannot be recovered from the aqueous or vitreous (Bach and Gürber, Stülp, Tornatola and Alessandro, Addario, Vogel). The most accurate experiments by Jannasch's method prove that after injection of 1 c.c. of 1 in 1000 sublimate solution the quantity in the aqueous is less than 1 in 100,000. Stülp, and especially Mellinger and Bossalino, with non-diffusible substances, have shown that the material spreads throughout the neighbouring lymph-spaces, permeating the orbital tissues. In albino rabbits Indian ink may be observed through the retina, choroid, and sclerotic ophthalmoscopically as dark spots around the disc.

The action of drugs upon the conjunctival vessels may be observed directly. Atropin causes slight dilatation owing to paralysis of the muscle-fibres, but the effect is very slight and only demonstrable on minute examination. Cocain causes contraction of the vessels owing to its excitatory effect, whilst tropacocain is said to cause dilatation (Andogsky). Eserin causes slight vasoconstriction (Ad. Weber and Mohr). The strongest vasoconstrictor is found in suprarenal extract—

suprarenin, adrenalin. Peronin and dionin, derivatives of morphin, cause great conjunctival œdema (Wolffberg).

As regards the moistening of the conjunctiva the effects of extirpation of the lacrymal gland show that the conjunctiva is itself capable of supplying a sufficiency of fluid. The absence of epiphora after extirpation of the lacrymal sac shows that under normal conditions the conjunctival mechanism is alone called into play, the lacrymal secretion being reserved for emergencies. The epiphora of dacryocystitis is doubtless due to reflex secretion from the gland, caused by the acute conjunctival irritation.

Massart endeavoured to ascertain the osmotic coefficient of tears by determining the concentration of salt solution which had no irritating properties. This somewhat crude method resulted in values of 1·32—1·46 per cent. NaCl. According to Muck, tears, like saliva, contain rhodan, and he attributes the conjunctival irritation which follows the administration of potassium iodide in some people to the presence of this substance.

The flow of tears, aided by the movements of the lids, has an important effect on the number of organisms in the conjunctival sac (Leber, van Genderen Stort). The tears seem, however, to be not only a bad culture medium for bacilli, but to contain substances which are actually deleterious to their growth (Bernheim, Bach, de Bono and Frisco, Valude, Helleberg). This is especially the case with *Staphylococcus aureus*, but not with tubercle or anthrax bacilli. The effect is diminished by prolonged heating at 58° C., and is probably due to the presence of alexins or anti-bodies.

Coccius.—Die Ernährungsweise der Hornhaut, 1852. Donders.—B. d. o. G., 1864; Jahresbericht d. Utrechter Augenklinik, 1864. Balser.—Deutsche Z. f. Chir., vii, 1876. Preiss.—Virchow's Archiv, lxxxix, 1882. Friedenwald.—C. f. A., xii, 1888. Sergejew.—C. f. d. med. Wissenschaft, 1894; Neurol. Centralbl., 1894. Schleich.—K. M. f. A., xl, 1902. Augstein.—B. d. o. G., 1902; Z. f. A., viii, 1902. Kämmerer.—Virchow's Archiv, lx, 1874. Alsberg.—A. f. A., ix, 1880. Leber—In G.-S., 1903. Römer.—C. f. A., xxiv, 1900. Mayer.—Wiener med. Woch., 1901. Stock.—K. M. f. A., xl, 1902. Pflüger.—Soc. franç. d'O., 1891. Addario.—A. f. O., xlviii, 2, 1899. Wessely.—K. M. f. A., xl, 1902; Deutsche med. Woch., 1902. Stülp.—A. f. A., xxxi, 1895. Bach and Gürber.—A. f. O., xli, 1, 1895. Vogel.—A. f. O., xlix, 3, 1900. Mellinger and Bossalino.—A. f. A., xxxi, 1895. Andogsky.—Ann. d'Oc., cxxvi, 1901. Ad. Weber.—A. f. O., xxiii, 1, 1877. Mohr.—A. f. O., xxiii, 2, 1877. Wolffberg.—Woch. d. Therapie u. Hygiene d. Auges, 1899. Massart.—Arch. de Biol., ix, 1889. Muck.—Münchener med. Woch., 1900. Leber.—Internat. Congress, Heidelberg, 1888. van Genderen Stort.—A. f. A., xiii, 1891. Bernheim.—B. z. A., viii, 1893. Bach.—A. f. O., xl, 3, 1894. de Bono and Frisco.—Ann. di Ott., vii, 1899. Valude.—Internat. Congress, Utrecht, 1899. Helleberg.—Mittheil. a. d. Augenklinik zu Stockholm, 1901.

CHAPTER XIX

THE THEORY OF IMMUNITY

THE investigation of the processes which underlie the various forms of immunity to the action of toxic agents in the body has led to far-reaching results which have an important bearing upon nutrition, not only in its pathological, but also in its physiological manifestations. The researches of Metchnikoff and his colleagues at the Pasteur Institute, and of Ehrlich and his followers have thrown a flood of light upon cell-life, and though the subject is one of great complexity it can no longer be ignored in dealing with the problems of physiology and pathology. It is only recently that the influence of the theory of immunity has made itself felt in the domain of ophthalmology, almost entirely owing to the researches of Römer, himself a pupil of Ehrlich. In order that the relation of immunity to ophthalmic problems may be comprehensible it is necessary to give a brief account of the evolution of the theory, more particularly as enunciated by Ehrlich.

The fundamental peculiarity of living cells is the elective affinity which they exhibit for certain substances which are useful for their nutrition, the substances varying with the type of cell. Chemical and physical processes have hitherto failed to give a satisfactory explanation of this peculiarity. It is well known that synthetic processes occur in the metabolism of the cell. Substances which are available for the nutrition of the cell must be such as are capable of being assimilated and synthetically bound up in the cell. In order that this may occur chemical groups must exist in the cell and in the food-stuff which possess strong affinity for each other. These chemically active groups in the living protoplasm, which have a maximal affinity for definite groups in the food-substances, and which serve to anchor the latter to the cell, are called by Ehrlich *side-chains* of the protoplasm or *receptors*. According to the side-chain theory the specific nutrition of individual types of cells is due to the possession by the living protoplasm of atom complexes which are capable of linking on certain other atom complexes, thus adding them to the protoplasmic molecule.

The side-chain theory is founded upon the analogy of the benzene ring, in which, by the linking on of other chemical groups, the character of the substance is entirely changed, though the benzene nucleus remains intact. Ehrlich first expounded the theory in 1888 in a book upon the need of the organism for oxygen.

Antitoxins.—Ehrlich's fundamental proposition found its earliest

and most important application in explaining the production of anti-toxins. Antitoxins had already been prepared by methods which were almost entirely empirical; the rationale of their formation was merely a matter of conjecture. Their origin and the enormous quantities which it was possible to obtain in small volumes of serum had not yet been satisfactorily explained. It was natural to suppose that the toxin was directly transformed into antitoxin, but this failed wholly to account for the quantities produced. Their most striking feature was their specific activity. Diphtheria antitoxin protected only against diphtheria, tetanus antitoxin only against tetanus. This characteristic especially pointed to the direct transformation of toxin into antitoxin, a view which was held by Buchner and Metchnikoff. Facts which militated against this theory rapidly accumulated. Some of the more striking may be mentioned. Thus, one part of toxin might give rise to 100,000 parts of antitoxin (Knorr). An animal might be deprived of nearly the whole of its blood by bleeding, but after a short interval the antitoxin content of the newly-formed blood had reached its former level (Salomonsen and Madsen, Roux and Vaillard). Moreover, anti-toxins are present in the blood of quite normal animals—e. g. diphtheria antitoxin and tetanolysin antitoxin in horses, staphylotoxin antitoxin in man, etc. Everything pointed to the fact that antitoxin production was a function of the living organism.

The investigations were first put upon a sound basis by Ehrlich's experiments with ricin and abrin. These poisons, when administered to animals, lead to the production of specific antitoxins, and Ehrlich succeeded in obtaining accurate quantitative estimates of the relationship between the dose of poison and the degree of immunity. From his experiments Ehrlich was led to apply his side-chain theory to the explanation of the problem. The bacterial poisons are substances which nearly approximate to proteids in their chemical constitution. Individual poisons possess atomic groupings which correspond with those of certain food-substances. When such a poison is introduced into the body the possibility arises of the toxin entering into direct chemical relationship with the protoplasm of suitable cell types. If the toxin possesses groups which are identical with those of the food-stuff, it will become chemically anchored to the protoplasm. Ehrlich went a step farther, enunciating the essential axiom of the theory of immunity. Directly the toxin is anchored to a receptor the latter can no longer fulfil its physiological function. If the function of the cell is not so severely affected as to cause the death of the cell, its protoplasm possesses the capacity of replacing the disabled side-chain. Not only so, over-compensation occurs, and more receptors are formed than are essential to the metabolic functions of the cell. This is especially the case when the stimulus is repeated, as is effected in immunisation by renewed doses of toxin. Finally, a time is reached when so many receptors are produced that they form an encumbrance to the cell. They are then cast off into the blood. Since they still retain the atom-complex which enables them to anchor the toxin, they now act as antitoxin. In the words of v. Behring, "the same substance in the living body which, when present in the cell, is the postulate and condi-

tion of poisoning becomes the cause of cure when circulating in the blood-stream."

The next problem to be solved was the nature of the action of the toxin upon the antitoxin. If a certain dose of diphtheria toxin in bouillon is injected into a guinea-pig the animal dies with characteristic symptoms. If, previously, a sufficient dose of antitoxin has been injected, the animal remains healthy. The same result occurs if the toxin and antitoxin are mixed before injection. No change is seen to occur in the serum when the mixture is made. An antitoxic serum is apparently exactly like a normal serum; indeed, v. Behring has shown that the antitoxin is absolutely harmless.

The first proof that the action of the antitoxin upon the toxin is a direct chemical combination was shown in Ehrlich's experiments with ricin. More striking, perhaps, were the later experiments of Martin and Cherry with diphtheria. If a diphtheria serum is passed through a gelatinised Pasteur-Chamberland filter it loses its antitoxic character. Diphtheria toxin, on the other hand, passes through such a filter with little loss of toxicity. If, therefore, a mixture of the two be passed through the filter, we may expect the filtrate to be toxic if the mixture is merely a mixture of the toxin with the antitoxin, whereas if the two have entered into chemical combination they may be expected to pass through intact. Martin and Cherry showed that the filtrate was absolutely innocuous.

The same investigators have proved, by another method, that chemical combination occurs. If Calmette's antitoxin to snake poison is warmed for ten minutes it ceases to be antitoxic; the same treatment has no effect upon the poison itself. Mixtures of the toxin and antitoxin were kept for thirty minutes at 20° C. After warming to 68° C. the mixture was found to be quite innocuous.

These and other such experiments prove also that the combination of the toxin with the antitoxin is independent of the organism, since it occurs equally well *in vitro*. Further, as in all chemical combinations, the law of multiples obtains. If 1 c.c. of antitoxic serum suffices to neutralise 100 lethal doses of poison, 3 c.c. will render 300 such doses inactive (v. Behring, Knorr, Ehrlich, Cobbet and Kanthack, Römer).

These researches negative the Roux-Buchner theory that the antitoxin has no direct action on the toxin, but acts upon the cells. Römer has confirmed the results in the actual presence of living cells by using the conjunctival sac as a test-tube. If a drop of jequirity solution is instilled into the conjunctival sac, the abrin contained in it causes the development of a croupous conjunctivitis after a short incubation period. If, on the other hand, a mixture of abrin solution and antitoxin, in such proportion that the toxin is neutralised and anchored to the antitoxin, is instilled, the eye remains as quiet as if physiological salt solution had been used. If the slightest excess of toxin is present inflammation results. Römer has elaborated the principle so as to afford a new method of quantitatively estimating the interaction of abrin and antiabrin. It may be pointed out that an animal cannot be immunised by such a neutral toxin-antitoxin mixture, since all the toxin is rendered ineffective, not only for

causing an inflammatory response, but also for stimulating the over-production of receptors which is the basis of immunity. The same mixture is neutral to any animal—whether injected into a mouse, instilled into the eye of a rabbit, or injected into the circulation of the highly susceptible guinea-pig.

From the clinical standpoint antitoxin has a double *rôle*—prophylactic and curative. The prophylactic effect is comprehensible on Ehrlich's theory from the circulation of large quantities of unsatisfied receptors in the blood-circulation. The curative effect is less easily understood. According to Metchnikoff the process is not brought to an end by the mere combination of toxin and antitoxin. The leucocytes are supposed to play an important part in making the organism proof against the toxin. The union of toxin with antitoxin simply raises the value of the toxin as a food material for the leucocytes. According to Ehrlich, however, the curative effect of the antitoxin is due to the ability of the antitoxin to dissociate the toxin from combinations which it has already made with the tissues of the body. As an example, the curative effect of tetanus antitoxin may be cited. Dönitz has shown that tetano-toxin is immediately taken up from the blood by the tissues, so that when a large amount is injected the lethal dose is fixed in four to eight minutes. The anchored poison is dissociated from the tissues by the antitetanus serum, is forthwith neutralised, and rendered innocuous. The dissociation is the more difficult the longer the interval between poisoning and the introduction of the serum. Although the toxin is fixed by the cells in a few minutes, yet cure may be effected after thirty minutes by the administration of five to ten times the neutralising dose of antitoxin. After a longer interval the strongest dose of antitoxin fails to save the animal.

Römer's experiments with abrin are of special interest to the ophthalmologist in this connection. By the administration of anti-abrin the inflammation produced by jequirity can be controlled. Not only is any free abrin which may be present neutralised, but that already combined with the tissues is set free and neutralised. Even more striking is the fact that the application need not be local to the conjunctival sac, for subcutaneous, intravenous, or intra-peritoneal injection effects the same result. Here it is obvious that the antitoxin circulating in the blood and lymph has the capacity of attacking the toxin fixed by the cells.

Careful consideration of the mode of action of organic toxins afford suggestive inferences as to the structure of the toxin molecule. Three features stand out prominently, viz. the specific activity of the toxin, its capacity to give rise to antitoxin, and the existence of an incubation period. The last fact emphasises the difference of toxins from most chemical poisons. For example, even if tetano-toxin is injected directly into the brain, the cells of which show a special avidity for it, yet a definite latent period occurs before poisoning sets in (Roux and Borrel). To explain this peculiarity, Ehrlich conjectures that every toxin molecule contains two different chemical groups—a haptophore group and a toxophore group. The *haptophore group* subserves the combination of the toxin molecule with the cell, which for its part possesses a

complemental unsatisfied group, viz. the receptor. The *toxophore group* is the nocuous element, which cannot exert its influence until linked on to the cell through the mediation of the haptophore group. On the side-chain theory the two groups are otherwise essentially independent.

The effect of the simpler chemical poisons, *e. g.* alkaloids, upon the cell is rapid and short-lived. The effect of organic toxins is slow and prolonged. They induce metabolic changes which modify the whole life-history of the cell: hence the analogy which Ehrlich delineated between their activity and cellular nutrition. Indeed, the analogy is very striking, especially when viewed in the light of Emil Fischer's experiments on ferment action. The activity of ferments is conditioned by the possession of a definite atomic grouping, which shows a specific avidity for a complemental atom complex in the substance attacked. Only such substances as possess the complemental group are subservient to the activity of the ferment, just as a lock can only be opened by a certain key. Further analogies are found in the physiological activity of definite atomic groups in synthetic hypnotics, anæsthetics, etc.—*e. g.* the ethyl group is prepotent in hypnotics, the benzoic acid group in anæsthetics.

As regards the toxophore group its enormous toxicity is noticeable: 0·0,000,004 gram of the tetanus poison is the lethal dose for a mouse. The next most notable feature is its lability, slight influences suffice to attenuate its activity. Most striking in this respect is the fact that the attenuated virus does not lose its capacity for producing antitoxin. Hence Ehrlich hypothecated a second, stable, haptophore group in the toxin molecule, and it is this group which not only conditions the anchoring of the toxin to the cell and so activates its toxicity, but also subserves the production of the antitoxin. This is shown by the fact that toxins whose haptophore groups are satisfied by antitoxin are no longer suitable for immunisation; they have lost their capacity for inducing the formation of antitoxin.

The experimental proof of the existence in the toxin molecule of two different groups was given by Morgenroth. He made use of the discovery by Courmont and Doyon (1892) that the frog, although insusceptible to tetanus at the ordinary temperature, became affected if kept at a raised temperature. This might be due to one of two causes: either the toxin did not become anchored to the nerve-cells at the lower temperature, or, though anchored, the toxic element was not capable of acting at this temperature. That the latter was the true explanation is shown by the fact that the longer the animal was kept in the cold after injection of the toxin the more antitoxin it was necessary to inject in order to protect it from tetanus on warming. Moreover, the same fact was confirmed by observation of the incubation period. Thus, the usual incubation time after raising the temperature is two to three days. Morgenroth kept frogs for twenty-four hours at 32° C., and then replaced them in the ice chest for days or weeks; on again warming them tetanus supervened after an incubation period which was never shorter than the normal by more than twenty-four hours. In other words, the cold interval was simply intercalated: on

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warming incubation went on exactly from the point at which it had been stopped. Hibernation has exactly the same effect (Billinger, Dönitz). The presence of two groups in the toxin molecule has also been shown by Neisser and Wechsberg's researches on staphylolysin, the poison formed by the staphylococcus which has the power of dissolving the hæmoglobin out of red corpuscles.

The facts and theoretical considerations which have hitherto been discussed apply to those toxins which are secreted by bacterial organisms and cast off into the surrounding medium—*e. g.* diphtheria, tetanus, etc. There are other pathogenic organisms which do not excrete the whole of their toxins, but keep them locked up in their own tissues—*e. g.* typhoid, cholera, plague, etc. Here the action of antitoxins is different and more complicated, but it is probable that they act as specific bactericidal agents. Two early hypotheses as to the cause of immunity in these diseases may be quickly dismissed. It was considered probable that the organism during the first attack used up all the available nutrient material, which it was supposed must be of a specific nature. Another view was founded on the fact that bacteria produce excretion products which have an inhibitory effect upon their own growth. As was proved by Flügge and his pupils, however, there is no evidence that any such products are retained indefinitely in the body. Finally, Metchnikoff attributes to the leucocytes the *rôle* of destroying the bacteria by ingestion.

In 1896 an important observation was made by Pfeiffer. If a subminimal lethal dose of typhoid bacilli, or a dose of bacilli mixed with serum from an immunised animal, is injected into the peritoneal cavity of a guinea-pig, and specimens of the peritoneal exudates are examined under suitable conditions, it will be found that in a few seconds after injection the bacilli have lost their motility. Moreover, they rapidly undergo changes in appearance. The bacteria become swollen and break up into granules, which soon dissolve entirely in the fluid, so that the number of organisms quickly diminishes. According to the Ehrlich theory this phenomenon is due to the presence of antitoxins in the fluid, though this is denied by Metchnikoff.

The analogy of the breaking up of bacteria to the well-known breaking up of red corpuscles under certain circumstances led to the latter phenomenon being carefully studied from this standpoint. There can be no doubt that the least exceptionable evidence in favour of Ehrlich's theory is to be found in the beautiful experiments which have been made on hæmolysis.

Hæmolysins.—It has long been known that the serum of many animals has the power of dissolving the hæmoglobin out of the red corpuscles of the blood of other animals, especially if the latter belong to a quite distinct species. The subject was investigated by Landois, and is responsible for the abandoning of blood-transfusion. In 1898 Belfanti and Carbone showed that the serum of horses became much more toxic to rabbits if rabbit's blood had been previously injected into the horses. Bordet attributed this to the formation of specific hæmolytic substances. He injected repeatedly 3—5 c.c. of defibrinated rabbit's blood into the peritoneal cavity of a guinea-pig; the serum of

this animal rapidly dissolved the hæmoglobin out of the red corpuscles of rabbit's blood *in vitro*, though normal guinea-pig's serum has little or no such power. Confirmatory experiments by Landsteiner and v. Dungern and others proved the extraordinary specificity of the reaction. It may be stated as a general rule that if the red corpuscles of one species are injected subcutaneously, intra-peritoneally, or intra-venously into another species the serum of the latter—"immunised"—animal becomes toxic to the erythrocytes of the former animal. It is clear that differences in osmotic pressure fail to explain the phenomenon, since a fraction of a milligram of serum cannot alter the tonicity of the fluid, as may indeed be proved by adding it to an isotonic saline solution. According to Ehrlich, hæmolysis is the sign of protoplasmic death in the stroma of the erythrocytes. It is usual to speak of the escape of hæmoglobin as solution of the blood-cells, though the stroma is not destroyed.

Further experiments showed that the analogy between antitoxins and hæmolysins extended to their chemical behaviour. Bordet found that if fresh hæmolytic serum was warmed to 55° C. and kept at this temperature for half an hour it became inactive. If a small quantity of normal guinea-pig's serum, which is also hæmolytically inactive, was added to this inactive serum it again became hæmolytic to rabbit's blood. Hæmolysis is therefore due to the presence of two substances, one of which is present preformed in the animal's serum, whilst the other is formed by the process of immunisation. Bordet called the thermostable element substance sensibilisatrice. It has since received many other names—preparator (Gruber), helping body (Buchner), copula (P. Müller), desmon (London), philocytase or fixator (Metch-nikoff), immune body or between body (Ehrlich and Morgenroth). Ehrlich has finally settled on the name *amboceptor*, which has been generally adopted. Bordet thought that the thermolabile substance was identical with Buchner's alexin, which is a substance in serum acting upon bacteria and foreign blood-corpuscles like an enzyme. It has since been called addiment, or finally *complement* by Ehrlich, and cytase by Metchnikoff.

It has already been mentioned that hæmolysins are specific. Thus, rabbit's serum immunised for guinea-pig's blood is only active to guinea-pig's erythrocytes; it will not dissolve sheep's erythrocytes. From this fact Ehrlich concluded that either the amboceptor or the complement possessed a specific affinity for some atom-complex in the red cell. Ehrlich and Morgenroth proved it in the following manner. A goat was immunised by injection of sheep's blood. The serum was warmed at 55° C., so that the complement was destroyed; 1·0 c.c. of this inactive serum was added to 4 c.c. of 5 per cent. sheep's blood; the mixture was kept at 40° C. for fifteen minutes and then centrifuged. To the clear fluid 0·2 c.c. of normal sheep's blood and 0·8 c.c. of normal goat's blood were added, and the mixture was kept at 37° C. for two hours. Not a trace of solution occurred. The sediment from the centrifuging was then washed in 4·0 c.c. of 0·85 per cent. salt solution and 0·8 c.c. of normal goat's serum was added; in two hours there was complete solution. The experiment proves that the amboceptor was

absorbed by the red corpuscles ; only on the addition of a small quantity of normal serum containing the complement was solution obtained. It was not, however, a simple absorption, for if so other red corpuscles might be expected to serve the purpose equally well. This was not the case, hence there is a definite specific chemical combination. The corpuscles can be repeatedly washed with physiological saline solution without causing any dissociation of the amboceptor from the cells. Quantitative experiments show that the amount of amboceptor anchored varies in different cases.

Ehrlich concludes from these experiments that the amboceptor possesses a haptophore group by means of which it becomes anchored to a receptor in the cell.

Corresponding experiments with the complement showed that this is not taken up by the corpuscles. Investigations carried out at different temperatures showed that the haptophore group of the amboceptor united with the receptor of the erythrocytes in the cold, whereas its affinity for the complement is less, and is only manifested at a higher temperature. It must, therefore, possess another haptophore group which is complementophile. Since the union of the complement can only be carried out by means of the cytophile and complementophile groups of the thermostable substance, this was suitably called the amboceptor. It finds its analogy in organic chemistry in diazobenzaldehyd. The analogy between a hæmolysin and a toxin scarcely requires to be pointed out : the haptophore group of the toxin is represented by the amboceptor, the toxophore by the complement. Bacterial hæmolysins have been described for pyocyaneus (Bulloch and Hunter), for streptococci (Basredka and Marmorek), for diphtheria (Lubenau), for typhoid (E. and P. Levy), etc. Snake poisons also contain hæmolysins (Stephens and Myers, Flexner and Noguchi).

It is unnecessary here to enter into the much-disputed question of the site of formation of the antitoxic and hæmolytic constituents. The specific nature of the amboceptor and the multiplicity of complements may be mentioned. The similarity of the complement to a ferment is emphasised in Metchnikoff's name—cytase. There is a striking parallel in the *rôle* of enterokinase in digestive processes and that of the complement in hæmolysis. It is not improbable that this fact may point the way to some general law of wide applicability, which will evolve order out of the chaos of these and similar difficult problems of physiology.

Neither is it necessary here more than to mention that hæmolysins may, under suitable conditions, give rise to antihæmolysins. Iso-hæmolysins and autohæmolysins, or bodies which cause solution of the hæmoglobin from the cells of the animals of the same species or of the same animal, have also been described : they, too, give rise to antibodies. Their importance can scarcely be exaggerated, but little is yet known about them.

The facts of hæmolysis have been utilised by Römer in attacking two problems of ophthalmology—one therapeutic, the other pathological. In the former hæmolysins have been injected into the vitreous in cases of intra-ocular hæmorrhage with a view to assisting in breaking up the red cells and promoting absorption. In some cases the results

have been favourable, but in others necrosis of the tissues has shown that the method is not without danger (Elschnig).

By the aid of hæmolysins Römer has brought forward the most delicate evidence against the ciliary nerve theory of sympathetic ophthalmia. According to this theory the irritation of the ciliary nerves in the exciting eye causes a sort of symmetrical irritation of the ciliary nerves of the other eye, so that the way is prepared for the sympathetic inflammation. If such irritation occur, it is to be expected that it will manifest itself by increased hyperæmia of the ciliary body, and this will be followed by the transudation of a more highly albuminous lymph than normal (*v. infra*, Chapter XX). Wessely investigated the problem by estimating the amount of proteid in the aqueous of each eye after one had been irritated severely. He found no increase in the second eye, and his results have been confirmed by Tornabene. Such experiments to decide so delicate a point are too crude to be of much value, since the error of experiment is probably fully as large as any alteration which might be reasonably anticipated. The hæmolysin test is far more delicate. Römer first confirmed the observation of earlier investigators that no hæmolysins are present in the aqueous of immunised animals—*e. g.* if a rabbit is immunised against ox-corpuscles by the injection of 15—20 c.c. of ox-blood into the peritoneal cavity the rabbit's aqueous will not dissolve ox-corpuscles. If, however, the aqueous is drawn off a second time after an interval of three quarters of an hour, it is powerfully hæmolytic. The delicacy of the test is shown by the fact that a milligram of the second aqueous will dissolve fifty or sixty million red corpuscles. Now, intense irritation of one eye does not cause the slightest trace of hæmolysin to appear in the normal aqueous of the other eye, whilst in every iritis and iridocyclitis, no matter how slight, hæmolysins are at once found in the aqueous of the first eye.

It was possible that the complement might already be present in the normal aqueous, whilst perhaps only the immunising body, the amboceptor, which in serum is chiefly attached to the globulins, entered with the regenerated aqueous. An exactly titrated hæmolytic serum was heated to 60° C.; hæmolysis only occurred if 0·01 active normal serum, containing the complement, was added to 0·0008 c.c. of this, which contained the amboceptor. It was found that even 0·2 c.c. of first drawn aqueous added to 0·0008 c.c. of the inactive immunised serum failed to cause hæmolysis. The complement was therefore not already present; it only appeared when the aqueous was regenerated. It was similarly proved absent from the first aqueous of the immunised animal. In an analogous manner it was also proved that the amboceptor was not already present in the first aqueous of the immunised animal. After puncture the complement appeared in the aqueous of the normal animal, and also the amboceptor in the immunised animal.

Römer further showed that the complement was present in the aqueous one hour after subconjunctival injection of 4 per cent. salt solution.

One eye was irritated by various means, a chip of copper in the anterior chamber, injection of dead typhoid bacilli or staphylococci into the vitreous, etc. In every case the first aqueous was hæmolytic

in the injured eye but not in the other. The same result followed chronic intra-ocular inflammation caused by the injection of a non-pathogenic culture of *Bacillus subtilis*. Further, although the second aqueous of the uninjured eye naturally contained hæmolysins, these disappeared in twenty-four hours. The experiments were also confirmed on monkeys immunised with ox-blood.

Bacteriolysins.—Reference has already been made to Pfeiffer's experiment (*v*. p. 1033). It is not my intention to enter into details as to the mechanism of bacteriolysis nor into the cognate question of bacterial immunity. It will be remembered that it is a matter here of organisms, such as typhoid, cholera, plague, pneumonia, etc., which exert their main influence, not by virtue of excreted toxins as do the tetanus and diphtheria bacilli, but by noxious properties contained in themselves. The subject is of enormous importance in the whole range of medicine, but chiefly from the prophylactic and therapeutic points of view.

It seems certain that the injection of dead cultures of the type of organism under consideration produces a definite reaction whereby the leucocytes are stimulated to increased bacteriolytic activity. The chemical stimuli which produce this result have been called *opsonins* by Wright.

It may be mentioned in passing that Römer has instituted a campaign in this field also. It has already been pointed out that the majority of cases of ulcus serpens are due to the pneumococcus. Statistical researches show that more than half the accidental wounds of the eye eventuate in ulcus serpens (Römer). Römer has shown that the eye can be protected against pneumococci by immunisation. As a prophylactic method the results are perfect in rabbits; as a curative method they are successful if the remedy is applied early. The immune serum is best obtained from rabbits, even when used for man. Römer maintains that early immunisation by anti-pneumococcic serum in man protects against the development of ulcus serpens, and that even progressive hypopyon ulcers can be brought under control.

Agglutinins, precipitins.—Agglutinins, which have an ætiological importance in general medicine, and precipitins, which bid fair to assume a preponderant *rôle* in forensic medicine, have not hitherto given evidence of much importance in ophthalmology. It is sufficient to mention here that, whilst receptors of the first order, such as serve to anchor toxins, ferments, and other cell secretions, possess only one haptophore group, those of the second order, which serve to bring about agglutination and precipitation, possess a haptophore group and a zymophore group. Agglutinins and precipitins pass readily into the aqueous; hence they are doubtless innocuous and are probably valuable as food material.

Cytotoxins.—The discovery of substances having a specific destructive influence upon red corpuscles naturally led to investigation as to the existence of specific poisons for other types of cells.

v. Dungern injected ciliated epithelium from the trachea of the ox into the peritoneal cavity of the guinea-pig. He found that the cells retained movement in their cilia for two days; in a week or so all the

cells had disappeared. A fresh dose of epithelium was injected ten to twelve days later. In eighteen hours all the cells had disappeared. Hence the animal had acquired a distinctly increased power of destroying the cells. Further research brought out the interesting fact that the serum of animals immunised against ciliated epithelium of the ox was hæmolytic to ox red corpuscles. Hence ciliated epithelium and erythrocytes must possess the same or nearly allied receptors. Even the injection of milk into a rabbit produced a serum which contained cytotoxins to ciliated epithelium and hæmolysins to ox blood.

An immense amount of work has been done on the same lines with spermatozoa by Metchnikoff and his pupils and others (Landsteiner, Moxter). The spermotoxic serum is also hæmolytic. On the other hand, Metalnikoff has shown that a hæmolytic serum produced by injection of blood is not spermotoxic, whilst the spermatozoa in a serum produced by simultaneous injection of spermatozoa and blood possesses the capacity of anchoring both the hæmolytic and the spermotoxic amboceptors.

Delezenne and Centanni have produced neurotoxins by the injection of brain-substance. Many other cytotoxins have been investigated— e. g. liver (Delezenne, Schütze, Deutsch, Hulot and Ramond), kidney (Bierry, Lindemann, and others), placenta-synzytiotoxin (Ascoli and others), ovary (Ceconi and Robecchi), suprarenal (Bigart and Bernard, Sartirana), pancreas (Surmont, Carnot, Garnier), stomach (Théohari and Babès, C. Bolton), pituitary body (Collins), thyroid (Gontscharnkoff, Mankowski, Sartirana).

More interesting to ophthalmologists are the conjectures of Römer as to the cause of senile cataract deduced from the side-chain theory. He compares the lens to a red corpuscle, each having a surrounding membrane which impedes the diffusion outwards of important constituents. When the hæmoglobin has passed out of the erythrocyte the cell is dead ; so, too, cataract is the expression of the protoplasmic death of the lens-fibres. Previous observations in hæmolysis have shown that isohæmolysins can be formed—e. g. in the goat (Ehrlich and Morgenroth); autohæmolysins, on the other hand, are only formed under pathological circumstances. If autocytotoxins occur it might be expected that they would be a sign of senile change, for atrophy and degeneration of tissues are the common features of old age. Now, it is necessary, if lentotoxins occur, that they should be able to reach the lens, or rather that the lens should be protected from them under normal circumstances. Hence the importance of knowing the behaviour of the secretory apparatus of the eye with regard to such bodies. It may be pointed out here that the essential feature of cytotoxin activity is its fixation by the cell; this has nothing to do with the osmotic conditions, but as soon as the cell is poisoned osmotic processes will have free play.

It has already been mentioned that neither constituent of hæmolysin, neither amboceptor nor complement, is present in the aqueous either of the normal or the immunised animal. Receptors of the second order, viz. agglutinins (Metchnikoff, Wessely, Römer) and precipitins (Römer), pass freely through into the aqueous. These, however, do

not act as cytotoxins, for the latter are always receptors of the third order—*i. e.* amboceptors with two haptophore groups, one cytophile, the other complementophile. Teleological considerations would lead one to suppose that substances of this type are not suited for nutrition of the lens and vitreous.

Römer has succeeded in showing that there are receptors of the second order in the lens—*i. e.* such as possess a haptophore and a zymophore group, and may be distinguished by their agglutinative properties. He has further shown that there are receptors of the first order present—*i. e.* such as possess a haptophore group which is capable of combining with substances of the type of toxins, ferments, and other cell secretions. He has also shown that there are complementophile receptors in the lens, and that these exhibit definite specificity. The experiments are too complicated for minute consideration here ; they must be studied in the original communication. They tend, however, to support the theory that senile cataract is a result of the specific activity of lentotoxins.

Römer has recently investigated the question of retinal cytotoxin. Cytotoxins as a cause for cyclitis is a thesis which has not yet been investigated, but would appear *à priori* to be specially likely to give affirmative results. These curiously insidious cases give every sign of toxic activity. In many cases a septic focus can be found in some part of the body, especially in the mouth—pyorrhœa alveolaris, etc. Here, doubtless, the cyclitis is the result of a bacterial toxæmia. In other cases in which no cause can be discovered it is not improbable that the essential factor is a specific cyclotoxin.

In my opinion, however, the work which has been done on cytotoxins in general is the weakest part of the structure which has been built on the basis of the side-chain theory. It is impossible at present to attempt to correlate the isolated facts which have already accumulated. It may be expected that further research, and especially the valuable criticisms and investigations of the Metchnikoff school, will eventuate in the discovery of some general principle underlying these complex problems.

*RÖMER.—Die Ehrlichsche Seitenkettentheorie u. ihre Bedeutung f. d. med. Wissenschaften, Wien, 1904 (Bibliography) ; A. f. O., lii, 1, 1901 (Jequirity) ; A. f. O., liv, 1, 1902 (Ulcus serpens) ; A. f. O., lv, 2, lvi, 3, 1903 (Sympathetic Ophthalmia) ; A. f. O., lx, 2, 1905 (Senile Cataract). HESS AND RÖMER.—A. f. A., liv, 1906 (Retina). ELSCHNIG.—Z. f. A., xi, 1905. *METCHNIKOFF.—Immunity in Infective Diseases, trans. by Binnie, London, 1905.

CHAPTER XX

THE NORMAL INTRA=OCULAR PRESSURE

THE eye is an elastic capsule, approximately spherical in form, the contents of which exert a pressure upon the walls which is greater than the surrounding atmospheric pressure; this pressure is the normal intra-ocular pressure.

The intra-ocular pressure and the tension of the walls of the globe are not the same, though the former varies directly with the latter. Supposing the globe to be a sphere, ab and ab' (Fig. 697) being two small segments; then if ab represents the force tending to move a towards b, and ab' the force tending to move a towards b', ab will be equal to ab'. By completing the parallelogram $abcb'$, the forces ab, ab' can be each resolved in two components represented by ad and bd, and ad and $b'd$ respectively. The components bd and $b'd$ are equal and opposite, so that only the vertical components $2\,ad$ or ac are equal to the internal pressure.
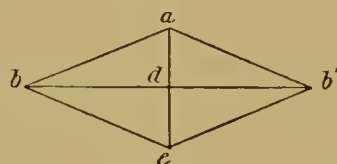
FIG. 697.

The relationship between the tension and intra-ocular pressure can be easily determined (Imbert, Fick). The following is Fick's proof, slightly modified by Leber. Let bb' (Fig. 698) be a small segment of the surface, and let ab, ab' represent the forces tending to move a towards b and b' respectively ; let c be the centre of the sphere. Then $< abd = < acb = \phi$, and $ad = ab \sin \phi$.

Let T be the tension in the unit of length, represented by ab, and T′ the component of T normal to the surface ; then

$$T' = T \sin \phi.$$

This tension, however, acts not only in the meridian shown in the figure, but in all meridians, and over an area represented by a circle with bd as radius, Now—

$$bd = bc \sin \phi.$$
$$= r \sin \phi.$$

Therefore the whole tension in this segment of the sphere—

$$S = T\,2\,\pi\,r \sin \phi.$$

The sum of the components normal to the surface—

$$S' = S \sin \phi.$$

Therefore—

$$S' = T \, 2 \, r \sin^2 \phi \, \pi.$$

Again, let P be the intra-ocular pressure, and P′ its components normal to the surface on a circle with radius bd.

The area of the circle with bd as radius—

$$= \pi \times (bd)^2 = \pi \, r^2 \sin^2 \phi.$$

And—

$$P' = P \, r^2 \sin^2 \phi \, \pi.$$

But—

$$S' = P'.$$

Therefore—

$$T \, 2 \, r \sin^2 \phi \, \pi = P \, r^2 \sin^2 \phi \, \pi.$$

Therefore—

$$T = \frac{Pr}{2}.$$

It follows from the above formula that the tension in different eyes will be different with the same intra-ocular pressure according to the length of the radius—*i. e.* to the size of the eyes. Moreover the tension will vary with the radius of curvature in different meridians (Jays).

Further, it is seen that the relationship between tension and pressure is independent of the co-efficient of elasticity of the walls. On the other hand, the stretching of the walls is directly dependent upon the co-efficient of elasticity ; the less the elasticity the greater will be the stretching. The elasticity of the walls of the eye is so great that the stretching under normal physiological pressure is minimal (v. Schultén, Koster Gzn).

Attempts have been made to estimate the elasticity of the cornea, sclerotic, etc., by measuring the increase of length in strips under different weights (Schelske, Ad. Weber, Ischreyt). The results are discordant. The cornea is more extensile than the sclerotic, and different parts of the sclera cut in different directions give very variable results. More reliable

FIG. 698.

results have been obtained by measuring the increase in volume of the intact globe under increments of intra-ocular pressure (Koster Gzn). The following is such an experiment from a fresh human eye :
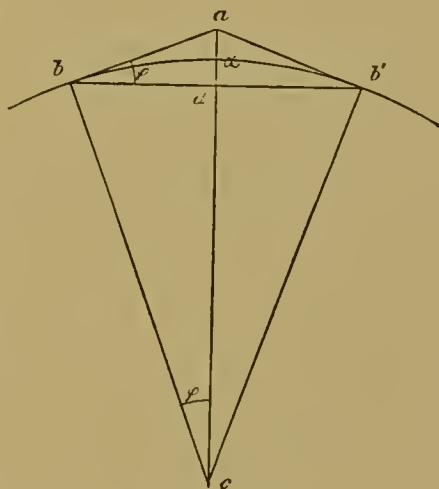
Pressure in mm. Hg.			Absolute increase in vol. in c.mm. per mm. Hg. increase in pressure.			Increase in vol. per mm. Hg. compared with total vol. of contents of globe (taken at 6500 c.mm.).
0	.	.	9	.	.	0·0014
7	.	.	4·5	.	.	0·007
9	.	.	2·25	.	.	0·0003

Pressure in mm. Hg.	Absolute increase in vol. in c.mm. per mm. Hg. increase in pressure.	Increase in vol. per mm. Hg. compared with total vol. of contents of globe (taken at 6500 c.mm.).
13	1·5	0·00023
19	1·0	0·00015
32	1·3	0·0002
70	0·9	0·00013

If therefore the intra-ocular pressure were raised from 19 mm. Hg. to 70 mm. Hg. the increase in the volume of the globe would be only about 45 c.mm., or $\frac{7}{1000}$ of the original volume. A sphere containing 6500 c.mm. would have a radius of 11·579 mm.; an increase in volume of 45 c.mm. would increase the radius to 11·606 mm.—*i. e.* by 0·027 mm., a quite inappreciable amount. The effect is still less when one considers that the normal intra-ocular pressure is about 25 mm. Hg.

Koster's experiments also show that the stretching is not proportional to the pressure, but becomes continually less with increasing pressure. This is due, not only to the constant condition which holds good for all elastic organised bodies, but also to the fact that the eye is by no means an exact sphere. Of all solid bodies the sphere has the greatest volume for a given superficies, hence it is to be expected that uniformly distributed increased internal pressure will tend to more nearly approximate the eyeball to a perfect sphere. It has, indeed, been shown by Helmholtz and others that increased intra-ocular pressure causes changes in the curvature of the cornea which are to be attributed to this effect; for normal or nearly normal pressures, however, the change is minimal.

Koster has examined the change in shape of the eye under different pressures. In rabbits' and pigs' eyes he found that under physiological pressures only the sagittal diameter became increased; very high pressures, up to 175 mm. Hg., caused no further noticeable change. The shape of the human eye was investigated by taking plaster casts. The following are the results obtained in one case:

	Pressure—3 mm. Hg.	10 mm. Hg.	25 mm. Hg.	100 mm. Hg.
Antero-posterior diameter	24	25	25·25	25·25
Vertical equatorial	26	26	26	25·5
Horizontal	26·5	26·75	26·5	26·25

Hence, with low pressures only the sagittal diameter shows appreciable change, whilst with high pressures practically no further change occurs.

Ophthalmometric observations of the curvature of the cornea afford a delicate means of determining the relationship to increased intra-ocular pressure. Such observations have already been referred to in treating of astigmatism (*v.* p. 936). Though it has been placed beyond dispute that changes in curvature occur, no simple or constant relationship to the height of the intra-ocular pressure has been made out.

The sclerotic possesses a high co-efficient of elasticity, and it is this membrane which supports the intra-ocular pressure. The choroid and retina do not contribute in any appreciable extent. Thus, if a window

be made in the sclerotic the choroid and retina bulge through the opening. Straub considered that this was due to the movable choroid being pushed into the aperture from the sides, and that it did not occur where the choroid was fixed as between the limbus and the vortex veins. Koster has shown that this view is not accurate.

Nicolai attributed some part in resisting the intra-ocular pressure to the retina. He showed that the retina is thicker if an eye is punctured before placing it in fixing fluid than if it is unopened, owing to relief from the stretching effect of the internal pressure. The true explanation, however, was brought forward by Koster, who pointed out that the tension inside the retinal tissue is equal to that outside. At death the tissue tension sinks to zero, whilst the intra-ocular pressure maintains a height of 9—10 mm. Hg. for a considerable time. Hence, in the unpunctured eye the retina will be compressed and the rods and cones will be arranged obliquely to the choroid. If the eye was previously glaucomatous both effects will be exaggerated, as has, indeed, been frequently observed.

The intra-ocular pressure is obviously a function of the volume of the contents of the globe. The solid part of the tissues being constant, variations in internal pressure must be due to changes in the amount of fluid. The fluid constituents are blood and lymph, and both vary in volume. As has already been pointed out (v. p. 967), there are two theories of lymph-production in the eye—(1) that the lymph is a true secretion; (2) that it is a filtrate from the blood. According to the former theory the intra-ocular pressure might vary independently of the blood-pressure; it might even exceed the blood-pressure, just as the pressure of salivary secretion may be made to exceed the pressure in the carotid artery. The only evidence which has been adduced in favour of the secretory theory is anatomical; all physiological evidence is consonant with the filtration theory. On these grounds the intra-ocular pressure is to be regarded as directly dependent upon the blood-pressure; under no circumstances can the former exceed the latter.

IMBERT.—A. d'O., v, 1885. R. A. FICK.—Dissertation, Würzburg, 1888; Sitzungs-bericht d. Phys.-med. Gesellschaft, xxii, 1888. JAYS.—A. d'O., vii, 1887. v. SCHULTÉN.—A. f. O., xxx, 3, 1884. KOSTER GZN.—A. f. O., xli, 2, 1895; xlix, 2 and 3, 1900; lii, 3, 1901. SCHELSKE.—A. f. O., x, 2, 1864. AD. WEBER.—A. f. O., xxiii, 1, 1876. ISCHREYT.—A. f. O., xlviii, 2 and 3, 1899. STRAUB.—A. f. O., xxxv, 2, 1889. NICOLAI.—Internat. Ophth. Congress, Utrecht, 1899. *LEBER.—In G.-S. ii, 2, 1903.

There are two methods of measuring the intra-ocular pressure—by the tonometer or by the manometer. The latter method, which is alone accurate, requires perforation of the globe, and is therefore not available as a clinical procedure.

In *ophthalmotonometry* the degree of internal pressure is estimated by the amount of resistance to deformation of the walls of the globe. Clinicians are accustomed to rely upon palpation or *digital tonometry* for rough estimates of intra-ocular pressure. Tactus eruditus enables one to distinguish with considerable accuracy various degrees of tension; these may be grouped into normal, slightly raised or lowered, moderately raised or lowered, and strongly raised or lowered. Bowmann introduced the conventions Tn, T + 1 or − 1, T + 2 or − 2, and T + 3 or − 3

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to represent these subjective impressions. A moment's consideration will show that this is a fundamental misuse of numbers, since there is no numerical relationship between various observations. These subjective indications should be replaced by pure conventions, such as Tn, T + or T −, T + + or T − −, T + + + or T − − −.

The attempt has been made to arrive at greater accuracy by *instrumental tonometry*. Instruments have been constructed on two principles —impression tonometers and applanation tonometers.

Impression tonometers measure either the depth of the impression or dimpling of the globe produced by a given force or the force which is necessary to produce an impression of a given depth. They have been invented by v. Graefe, Hamer (modified by Lecoultre), Donders, Monnik, Lazerat, Priestley Smith, Helmbold, and Snellen. It is true that the depth of the impression varies inversely with the internal pressure of the eye, but there are also so many other variables that the method is highly inaccurate. Thus, the deformation is dependent upon the curvature of the surface, which varies not only in different eyes but in
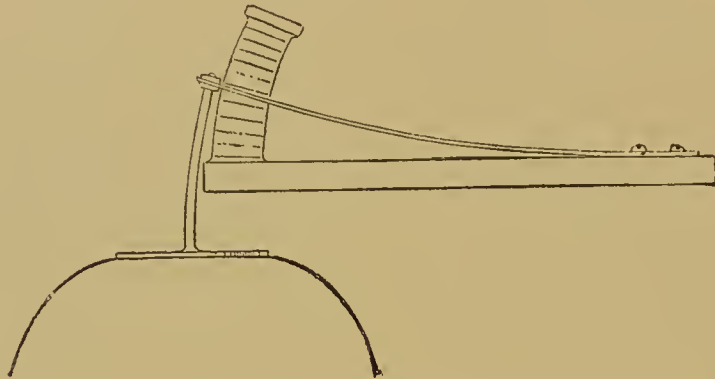
FIG. 699.—FICK'S TONOMETER.
From Priestley Smith.

different parts of the same eye; it also depends on the extensibility of the membrane. There are other factors which interfere with the accuracy of all tonometers—*e. g.* any pressure upon the globe necessarily increases the internal pressure.

Applanation tonometers are more accurate. They depend upon the principle that

$$p = J + N,$$

where p is the pressure applied externally, J the component of the intra-ocular pressure acting on a given area, and N the vertical component of the tension of the walls acting upon the same area. N varies in a manner which cannot be measured with accuracy, but it was shown by Ad. Weber (1868), Imbert (1885), and A. Fick (1888) that it can be eliminated. It has been already pointed out that the vertical component of the tension of the wall over a small area is represented by ae (Fig. 697). If the surface is pushed inwards so that the concavity is equal to the former convexity the vertical component will be represented by ac acting in the opposite direction. Therefore if the wall be simply flattened, so as to assume the position bb', the vertical component will

be eliminated and the horizontal components will be equal and opposite. Under these circumstances

$$J = P = s.h.f,$$

where J is the weight of a column of mercury equal in height to h, the intra-ocular pressure, and with a surface equal to f, the area flattened; P is the weight in grammes applied externally, and s is the specific gravity of mercury.   Therefore

$$h = \frac{P}{s.f} = \frac{P}{s.\pi r^2}$$

—i.e. the intra-ocular pressure is directly proportional to the external pressure and inversely proportional to the area flattened.

In order that the results may be accurate the area must be exactly
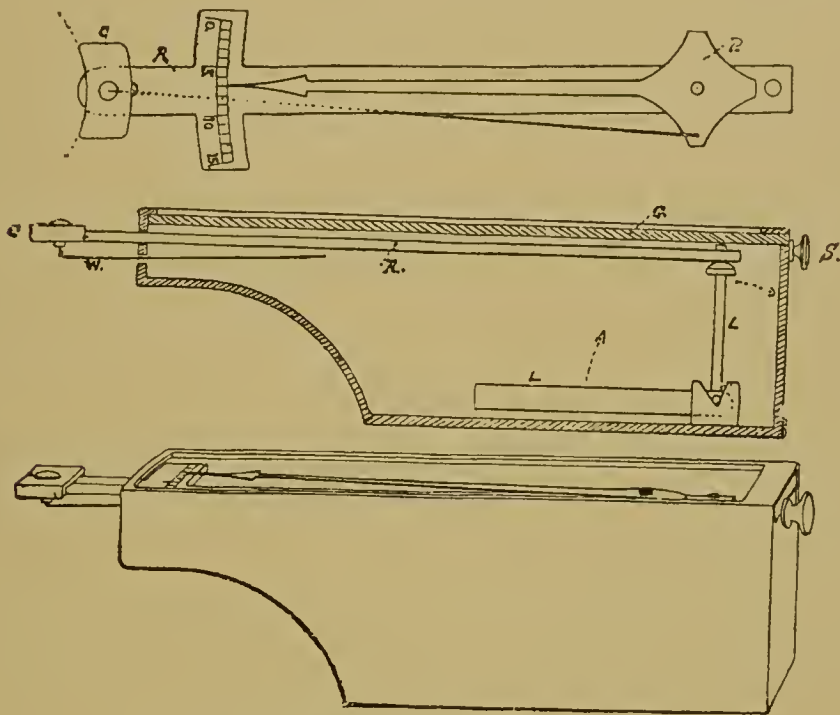
FIG. 700.—PRIESTLEY SMITH'S TONOMETER.

The ram, R, carries the crescent, C, and the pointer, P, the crescent and pointer being connected by a wire.   The end of the ram rests on the upright arm of a rectangular lever, L.

flattened; if it is depressed the surrounding wall will rise sharply round the circumference and the reading will be too low.   Theoretically the wall must be linear, so that the thickness—and especially the variations in thickness—of the wall of the eye introduces an error (Koster Gzn), which is, however, comparatively small.

It is obvious that instruments of two kinds can be constructed upon this principle, viz. those in which the external pressure (P) is constant and the area depressed (f) is measured, and those in which the f is constant and P is measured.   The tonometer of Maklakoff (1885) belongs to the first type, that of A. Fick (1888), modified by Koster (1895) and Ostwalt (1895) to the second.   It is unnecessary to describe these instruments here since they give only relatively con-

cordant results, both on account of the reasons already given as well as owing to the variations in flexibility of the sclerotic, the thickness of the conjunctiva or the danger of application to the cornea, difficulties of employment, etc.

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In *ophthalmomanometry* the intra-ocular pressure is measured directly by connecting the interior of the eye with a manometer. At the cost of a little repetition it is advisable to review briefly the anatomical, physical, and physiological conditions which obtain.

The ophthalmic artery, from which the whole of the blood-supply of the eye is derived in man, is a branch of the internal carotid within the cranium. It is therefore a direct offshoot from the intra-cranial circulation, and much stress has been laid upon this fact clinically, so that the condition of the retinal arteries has been assumed to be a criterion of the circulation within the skull. More minute investigation of this question, however, educes many facts which so seriously modify such an assumption that it can only be accepted with severe limitations.

After traversing the orbit without, so far as is known, having any large or important communication with extra-cranial blood-vessels, the branches of the ophthalmic artery which are distributed to the eye enter the globe, and are then placed under special physical conditions. Like the arteries which enter the cranium, they, too, enter a closed box. Unlike the cranium, however, the eyeball is not a rigid case, but is capable of variations in form according to the forces which are brought to bear upon it, either from without or from within. Under normal conditions, the fluid contents of the globe exert a pressure of 20 to 30 mm. Hg. above the atmospheric pressure, which may be regarded as the measure of the external pressure when the eye is at rest. The blood-vessels which enter the eye, therefore, are now subjected to an increased pressure of 20 to 30 mm. Hg. The blood-pressure in the ophthalmic artery has been measured by v. Schultén in the rabbit by inserting a cannula into the vitreous and driving in saline solution under known pressure until the blood-flow in the retinal arteries was just stopped, as observed ophthalmoscopically. It was found to be only a few (2 to 15) mm. Hg. below that in the large arteries (carotid or femoral). The capillary pressure in most parts of the body is normally about 15 to 20 mm. Hg. (Starling). No means has yet been devised for measuring the intra-ocular capillary pressure, since the veins are so small and anastomose so quickly and profusely after leaving the eye

that it is impossible to measure the venous pressure. It is just possible that this may be found feasible in the dog or some larger animal by utilising the communication with the angular vein and tying off the posterior communication with the cavernous sinus. In any case, it is clear that, with an external pressure—the normal intra-ocular pressure—of 20 to 30 mm. Hg. the capillary pressure must be considerably above this level, and we shall probably not be far wrong in considering it equal to 40 or 50 mm. Hg. It is most likely that this is the highest capillary pressure of any organ of the body whilst at rest, though many organs are doubtless subject to wide variations in this respect during activity.

We know that the outflow of blood from the eye by the veins is usually a steady stream. It therefore follows that the venous pressure must also be considerably above the average in other parts of the body,[1] since, if it were below the intra-ocular pressure, the veins would collapse, and would only be reopened when the internal pressure rose above that level. It has been thought that increase of intra-ocular pressure would tend to close the venæ vorticosæ, but experimental investigation does not bear out this view. The very oblique course of these vessels through the sclerotic is further a protective mechanism against kinking, such as might be produced by the action of the ciliary muscle in dragging forward the equatorial region of the choroid. As long as the intra-ocular tension is constant, the fluid contents of the globe must be constant, any outflow of fluid, either blood or lymph, being equalised by a corresponding in-flow or secretion. Under these circumstances, the eye is temporarily a rigid box, and as shown to be the case in the brain by Leonard Hill, the venous pressure is equal to the intra-cranial pressure, so here, too, the venous pressure will also be equal to the intra-ocular pressure. This will not hold for variations of intra-ocular pressure, as it does in the case of the brain, because under these circumstances the eyeball is no longer a rigid case.

The fundamental problem which requires solution is the mechanism which brings about the normal intra-ocular tension, and which constantly sustains it at so high a level. Unfortunately, the problem yet awaits complete solution. It is obvious that it is allied to the problem of secretion in other parts of the body, and more particularly to the production of lymph, for there can be no doubt now that the aqueous fluid, which is the essential factor, must be considered rather as lymph, modified by the peculiar conditions of its production, than as a secretion allied to saliva, etc. (v. p. 978). It may be argued that this does not simplify the question much; in one sense, however, it does. Like lymph, the secretions of the body are ultimately derived from the blood, but there is an increasing volume of evidence to show that they are more remotely dependent upon the physical conditions of the circulation than is the case with lymph. Thus, saliva can be secreted at a pressure far above the blood-pressure of the carotid artery; whereas even if lymph is produced by a "vital" secretory process, no such in-

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[1] Small veins of the arm . . . . + 9 mm. Hg.
Portal vein . . . . . + 10 „
Inferior vena cava . . . . + 3 „
Large veins of the neck . . . . o to − 8 „ (Starling).

consistency with the physical laws of filtration is observed. Indeed, the repetition of Heidenhain's work upon the subject by Starling has led to a reversal of the former's conclusions, so that the evidence is now rather in favour of a purely physical process in the production of lymph. Starling and Henderson have carried these researches into the domain of ocular physiology in recent experiments. Under normal conditions the aqueous contains a very small proportion of proteids—only about 0·045 per cent. These consist of serum albumin, serum globulin, and fibrinogen, the proteids of the blood. If, however, the anterior chamber is tapped, so that the intra-ocular tension falls to zero, the aqueous secreted now contains much larger percentages of the same proteids. This tends to show that the process of production is one of physical filtration, the reduction of pressure on the negative side of the membrane allowing the transfusion of greater quantities of the large-moleculed proteids. Extended researches have confirmed these results. Anatomical researches, such as the demonstration of "glands" in the ciliary body, by Treacher Collins, cannot be held to controvert these results; and the absence of these "glands" in many animals, e. g. albino rabbits, proves that they are not essential. At the same time, it is probable that here, and indeed in the whole domain of lymph-production, the question is not quite so simple as the physical theory supposes. What is of prime importance is the fact that everything tends to show that the secretion of aqueous is directly dependent upon the intra-capillary pressure, and that it varies *pari passu* with that pressure.

It has been already stated that there is no means at present of directly, or even indirectly, measuring the intra-capillary pressure accurately. We can, however, measure the intra-ocular tension, and if the deductions which have been already drawn are reliable, this will afford an index to the capillary pressure. So far with accuracy; beyond this, with regard more especially to the condition of the arteries, in the absence of any knowledge of the concomitant venous pressures, the deductions must remain somewhat conjectural. Since the venous pressures, with a few exceptions, to which attention will be drawn, are not likely to vary within wide limits, a rise of intra-ocular pressure may be regarded as equivalent to a dilatation of arterioles, a fall being equivalent to a constriction, for a rise of tension means increased fluid content. The increased fluid may be intra- or extra-vascular; in the former case it means dilatation of vessels, in the latter either increased production or diminished excretion of lymph. In general the changes during comparatively rapid observations will be due to vascular dilatation or constriction, for the variations of secretion and excretion are relatively slow. Even if they occur, they will generally be in the same sense as the vascular changes, and will not vitiate the results. Thus, increased production of fluid means increased intra-capillary pressure, which may be due either to increased arterial or increased venous pressure. The latter probably only occurs in specific cases, being caused either by increased general venous pressure or by mechanical constriction of the local veins. There is no evidence of physiological venous constriction, though it is by no means improbable that it may occur. Increased arterial pressure may be due to increased general

arterial pressure, the ocular arterioles remaining unchanged or more frequently dilating passively, or by local dilatation. Thus, the dilatation may be either a passive one, brought about by the constriction of other larger areas, notably the splanchnic area, or an active vaso-dilatation. In general, then, rise of intra-ocular tension under the given experimental conditions will be due to arterial vaso-dilatation, with certain definite exceptions.

These are the main considerations by which the results must be judged. There is yet, however, an important possibility which must be eliminated. If the walls of the eyeball were rigid, no change in the volume of its contents could occur—vaso-dilatation could only happen at the expense of vaso-constriction of an equivalent intra-ocular area, or by the expulsion of an equal volume of lymph from the eye ; in fact, the conditions would be identical with those found by Leonard Hill to obtain in the intra-cranial circulation, anticipated in theory by the Monro-Kellie doctrine. The effect of the elasticity of the walls of the eye has been already considered (v. p. 1040), and must be taken into account.
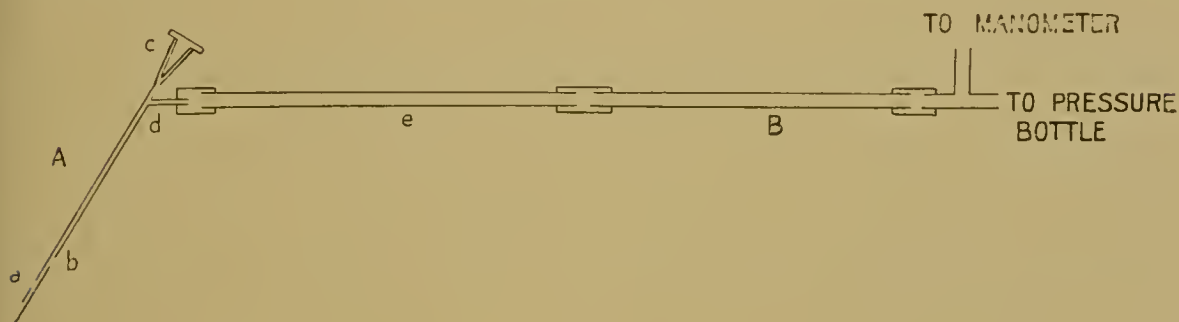
Fig. 701.—Intra-ocular Pressure Apparatus.
Parsons, The Ocular Circulation.   A. Cannula.   B. Horizontal tube for air-bubble.

Experience derived from the examination of human eyes with the ophthalmoscope afford an immense amount of evidence that very considerable changes occur in the volume of the arteries and veins of the retina, and that too in the absence of any pathological variations of tension. Changes may also occur physiologically, but the investigation of the human eye affords no proof that they are directly under the control of specific vasomotor nerves.

In order that the results may be accurate the technique of ophthalmomanometry demands that the internal pressure of the eye shall remain unaltered by the necessary manipulations. The first essential is therefore that no fluid shall enter or leave the eye whilst the cannula, by which the interior is placed in connection with the manometer, is being inserted. Repeated experiments have shown that the pressure in the anterior chamber is equal to that in the vitreous (v. infra). A priori, therefore, it is immaterial whether the cannula is inserted into the former or into the latter, but, as will be seen later, special precautions must be adopted if the vitreous chamber is used.

Various forms of cannula have been employed, differing only in minute

details. Of these the best is that introduced by Leber, or one constructed on the same principle. It consists of a sharp hollow needle with a lateral aperture about 9 mm. from the pointed (closed) end. The cornea is transfixed in such a manner that the lateral opening lies in the anterior chamber between the puncture and the counter-puncture. In my own experiments I employed a gilt hollow needle having two small lateral openings at *a* and *b* (Fig. 701) upon opposite sides near the pointed end, which is also open. This insures free communication with the interior of the eye. The distal end *c* is closed by a plug which can be replaced by a stylet for cleaning out any clot or other obstruction when the cannula is not in use. A side tube *d* near the distal end leads off to the manometer.
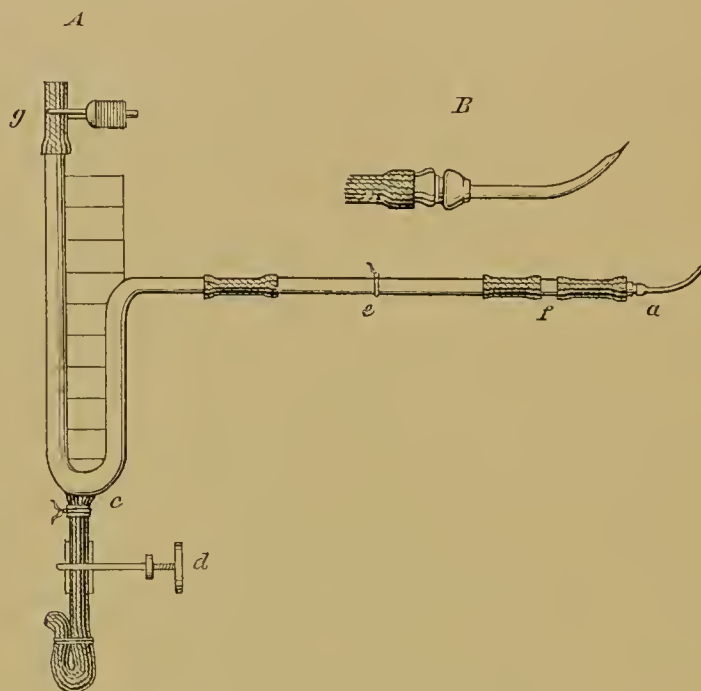
FIG. 702.—V. SCHULTÉN'S APPARATUS.

A. f. O., xxx, 3, 1884. *A, a.* Cannula. *B.* Cannula, natural size. *c.* Mercury manometer. *d.* Screw slip for compressing rubber reservoir. *e.* Horizontal tube for air-bubble.

Connection with the manometer and other parts of the apparatus should be made by flexible lead tubing or by thick-walled rubber tubing having a negligible amount of extensibility for the pressures under consideration. It is best to reduce the rubber connections to a minimum, and it is possible to eliminate them altogether, as in Leber's filtration manometer. The apparatus is filled with isotonic saline solution.

In order that no fluid may enter or leave the eye during the introduction of the cannula the pressure in the apparatus must be previously raised to the anticipated intra-ocular pressure. It is, of course, only possible to effect this approximately, but the error is not usually sufficiently great to vitiate the experiment. Various methods have been employed to indicate the entrance or exit of fluid from the eye, with a view to counteracting the error. The most convenient is that intro-

duced by v. Schultén, and employed by Bellarminoff, myself, and Starling and Henderson ; it was also employed by Bayliss and Hill in recording intra-cranial pressures. This consists of the interposition of a horizontal thermometer tube, into which a bubble of air is admitted. A scale is placed under the tube, so that any movement of the bubble
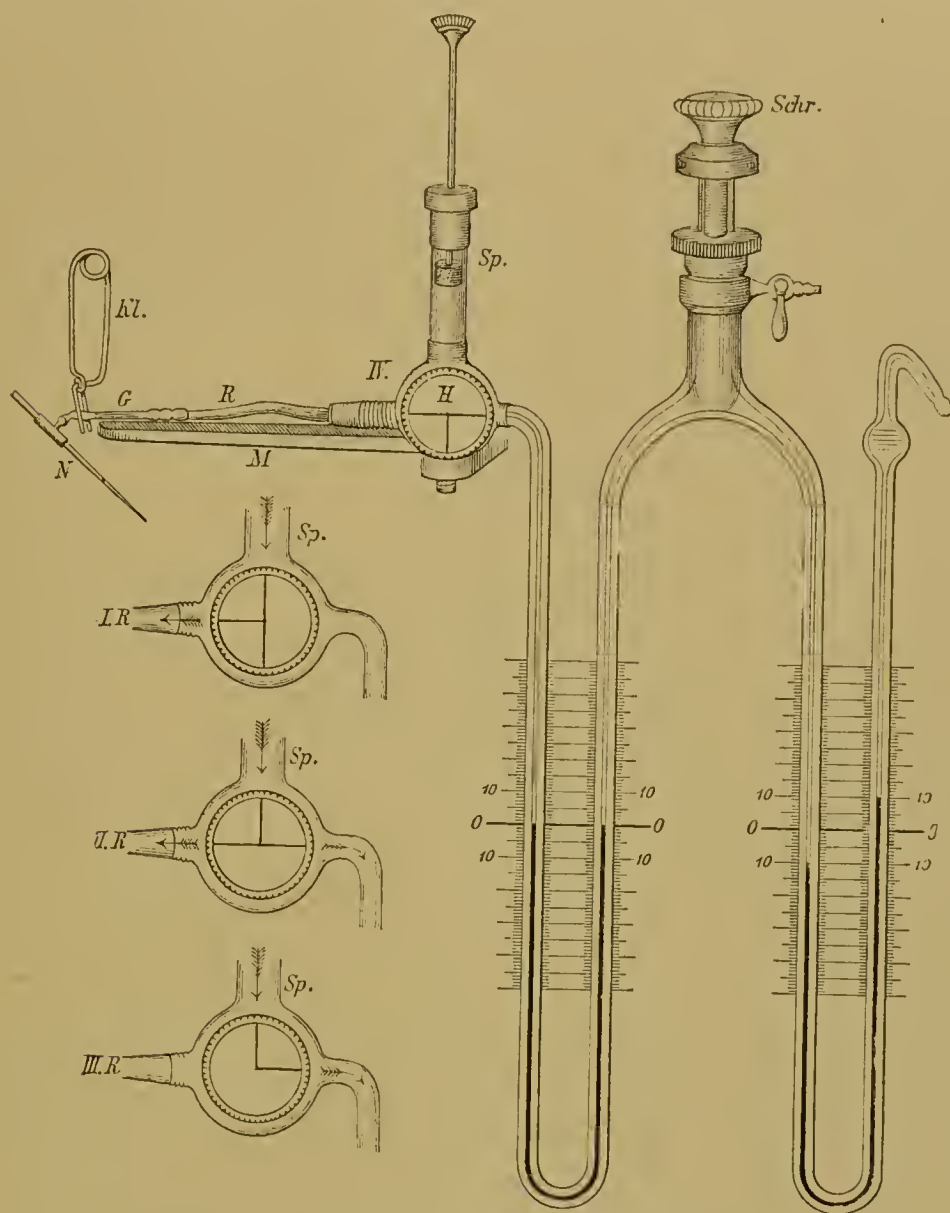
FIG. 703.—HÖLTZKE-RINDFLEISCH APPARATUS.
A. f. O., xxix, 2, 1883; xxxviii, 2, 1892. *N*. Cannula. *Kl*. Clip. *H*. Three-way tap. *I, II, III, IV*. Different positions of the tap. *Sp*. Syringe for keeping mercury level in the first manometer, which communicates with the second mano-meter giving the readings.

towards or from the eye indicates entrance or exit of fluid, which must be counteracted by altering the pressure in the system.   Another method, used by Höltzke, consists in interposing a second manometer, the mercury in the u-tube being kept at the same level in each limb by the compensating pressure apparatus.

The compensating pressure apparatus has also been varied by different experimenters. v. Schultén used a reservoir of mercury connected with the bottom of the u-tube of the manometer. By altering the pressure on the reservoir, which consisted of thick-walled rubber tubing, by means of a clamp, the pressure in the manometer could be varied so as to keep the bubble of air constant in the intervals of taking readings. Höltzke and Leber employed a syringe whereby fluid—saline or mercury—could be forced in or abstracted. I employed a pressure bottle exactly similar to that used in ordinary blood-pressure experiments, but filled with saline, and this method was also used by Starling and Henderson.

As regards the manometer most investigators have used an ordinary
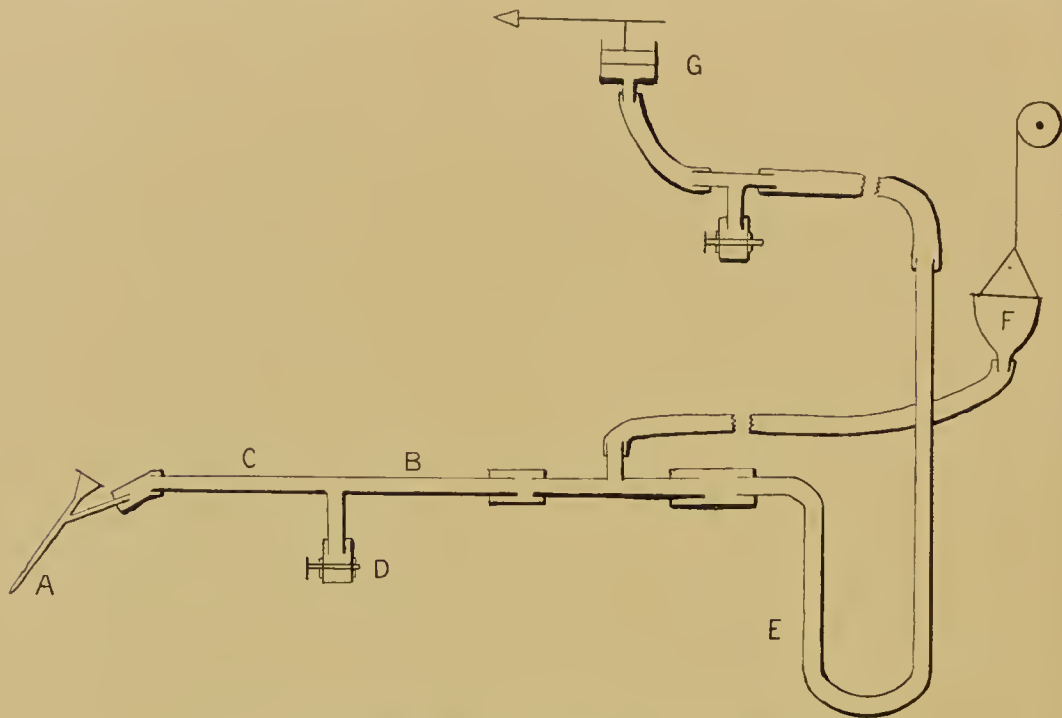
FIG. 704.—HENDERSON AND STARLING'S APPARATUS.

Henderson and Starling, Jl. of Physiology, xxxi. A. Intra-ocular pressure cannula, connected by pressure tubing with B, a piece of capillary tubing provided with a T-piece, D. Through D is introduced the air-bubble C. This serves as an indicator. The other end of the capillary tube is connected by means of a T-piece with the manometer, E, and the pressure-bottle, F. By adjusting the height of F to the various intra-ocular pressures no movement of the air-bubble is allowed to take place. G is a piston-recorder connected with the top of the manometer.

u-shaped mercury manometer (v. Schultén, Höltzke, Leber). In order to diminish the variations in volume of fluid in the eye during actual readings it is essential that the manometer tube should be narrow; Leber's was calibrated so that 1 mm. contained 1 c.mm. (diameter = 1·13 mm.). When it is only desired to obtain differential observations it is convenient to employ a graphic method; absolute readings can then be easily found by calibrating the apparatus. For this purpose I used a Hürthle manometer, provided with a thin rubber membrane, or an ordinary Marey tambour, about twice the diameter of the Hürthle, with a rather thicker membrane. Starling and Henderson used a water

manometer, filled with saline.   Bellarminoff obtained graphic records by photographing the movements of the air-bubble.

Utilising the various schemes already described, Leber constructed an ingenious filtration manometer, whereby not only the intra-ocular pressure, but also the rate of filtration or production of fluid in the eye, could be measured.

Hering's micromanometer consists simply of a capillary tube, closed at the top, filled above with air and below with saline.   This is connected directly with the cannula.   Changes in pressure compress or decompress the air, but the alterations in volume are so small that the
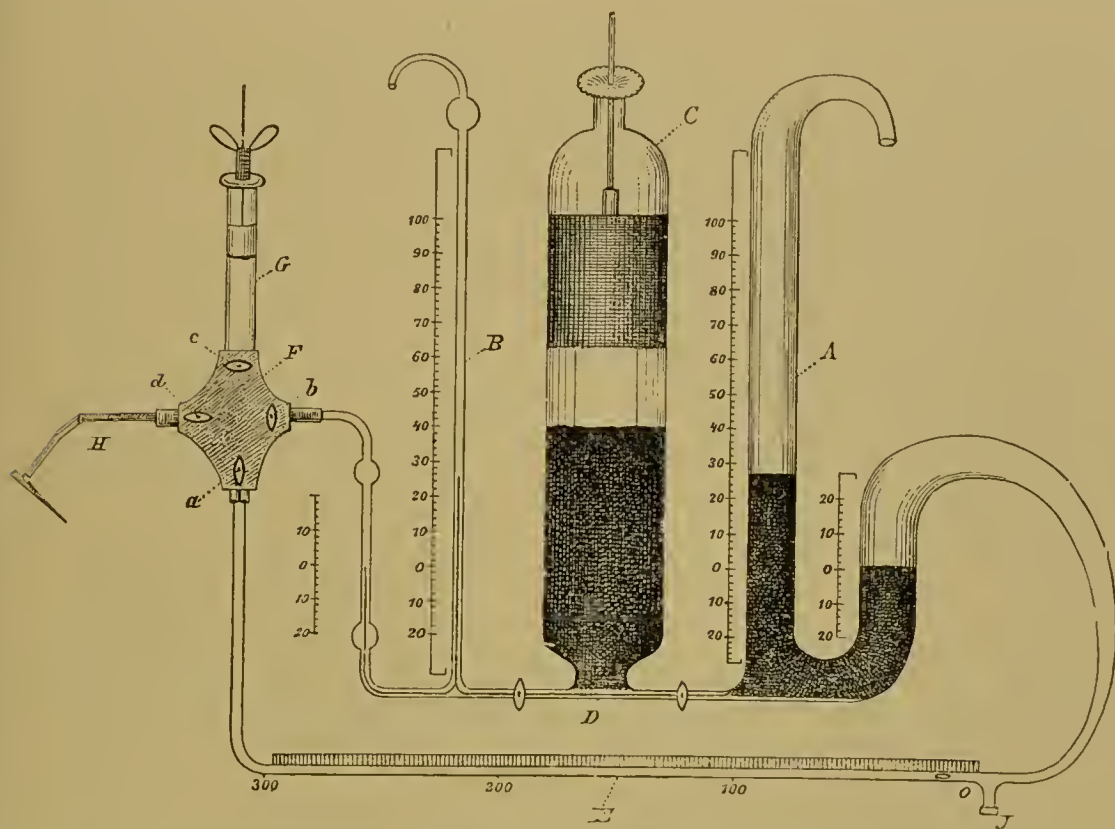
FIG. 705.—LEBER'S FILTRATION MANOMETER.

In Niesnamoff, A. f. O., xlii, 4, 1896.   This apparatus is used for measuring both the pressure and the rate of filtration. *B.* Narrow manometer for pressure readings. *C.* Mercury reservoir with piston, capable of raising the pressure in the wide-bored manometer, *A*, to 100 mm. Hg. *E.* Horizontal tube, 300 mm. long and 1 sq. mm. bore, for air-bubble. *G.* Pressure syringe. *a, b, c, d.* Four stop-cocks.

surface of the fluid must be observed with a microscope ; moreover, variations in temperature must be taken into account. .The instrument is useful for demonstrating the pulse and respiratory waves upon the pressure.

v. Schultén used a cannula introduced into the vitreous chamber. Koster Gzn showed that the viscous consistency of the vitreous impeded the free to-and-fro movements of the fluid in the cannula, and Grönholm found that the diameter of the lumen should be at least 1·5 mm.   Since v. Schultén's cannula had a lumen of only 0·75 mm. his results are somewhat vitiated.   A large cannula inserted into the vitreous causes more

disturbance than a small one in the anterior chamber, so that, unless the conditions of the research demand it, it is advisable to avoid this method. For comparison of the pressure in the anterior and vitreous chambers Hamburger used a differential manometer on principles derived from Ehrlich and Zuntz.
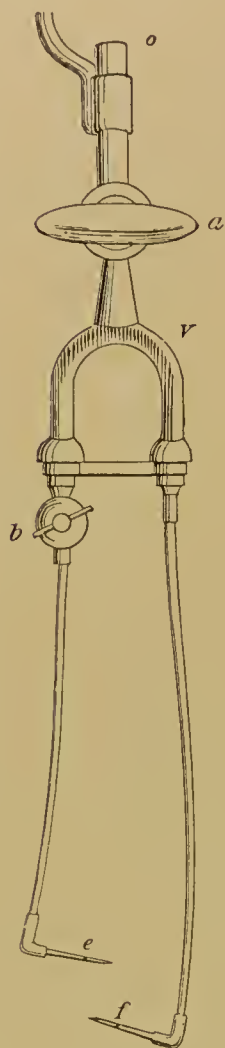
C. WEBER.—Dissertation, Marburg, 1860. WEGNER.—A. f. O., xii, 2, 1866. GRÜNHAGEN.—Z. f. rat. Med., xxviii, 1866. ADAMÜK.—C. f. med. Wissenschaft, 1866, 1867; Ann. d'Oc., lviii, 1867; K. M. f. A., vi, 1868. v. HIPPEL AND GRÜNHAGEN.—A. f. O., xiv, 3, 1868; xv, 1, 1869; xvi, 1, 1870. HERING.—In Adamük, Sitzungsberichte d. Wiener Akad., lix, 2, 1869. SCHÖLER.—Dissertation, Dorpat, 1869; A. f. O., xxv, 4, 1879. HÖLTZKE.—A. f. O., xxix, 2, 1883; Verhandl. d. phys. Ges. zu Berlin, 1884. v. SCHULTÉN.—A. f. O., xxx, 3, 1884. BELLARMINOFF.—Pflüger's Archiv, xxxix, 1886; Ann. d'Oc., xcvii, 1887; B. d. o. G., 1887. BÖDEKER.—Dissertation, Berlin, 1886. KOSTER GZN.—A. f. O. xli, 2, 1895; C. f. A., xxii, 1898. HAMBURGER.—C. f. A., xxii, 1898; xxiii, 1899. GRÖNHOLM.—A. f. O., xlix, 3, 1900. *PARSONS.—The Ocular Circulation, London, 1903. *HENDERSON AND STARLING.—Jl. of Physiology, xxxi, 1904. *LEBER.—In Niesnamoff, A. f. O., xlii, 4, 1896; in G.-S., ii, 2, 1903.

The normal intra-ocular pressure is about 20—30 mm. Hg. both in man and in the usual animals which are subjected to experimental research. According to Graser the pressure rises in any given species of animal with its size. The following are some estimates collected by Leber: in non-narcotised animals—Wegner, in rabbits, 26·5 mm. Hg.; Leber, 23·2 mm. Hg.; Niesnamoff, with cocain, 25 mm. Hg.; in cats—Höltzke, Graser, with A.C.E. mixture, 28·4 mm. Hg.; with morphia, 18·5 mm. Hg., with curare, 16·0 mm. Hg.; Adamük, with chloroform, 24·2 mm. Hg.; with curare—Grünhagen, 25·5 mm. Hg., v. Hippel and Grünhagen, with atropin also, 22—24 mm. Hg., Stocker, 28·5 mm. Hg.; in rabbits—with curare, Pflüger, 18 mm. Hg., v. Hippel and Grünhagen, 25—30 mm. Hg., v. Schultén, 22·5 mm. Hg.; with A.C.E. mixture, Stoker, 18—20 mm. Hg.; in dogs—v. Schultén, with curare, 24 mm. Hg.; Adamük, with opium, 19·5 mm. Hg. A single manometric observation on the human eye has been recorded by Wahlfors, using v. Schultén's method; the pressure was 26 mm. Hg. Numerous tonometric observations by Maklaloff gave a mean of 25 mm. Hg.

FIG. 706.—DIFFERENTIAL MANOMETER.
Hamburger, C. f. A., xxii, 1898. e, f. Cannulæ for anterior and vitreous chambers. b. Stop-cock. V. Glass U-tube, filled below with saline, above with petroleum.

LEBER.—In G.-S., ii, 1876. NIESNAMOFF.—A. f. O., xlii, 4, 1896. GRASER.—Dissertation, Erlangen, 1883. ADAMÜK.—C. f. d. med. Wiss., 1866. v. HIPPEL AND GRÜNHAGEN.—A. f. O., xiv, 3, 1868. STOCKER.—A. f. O., xxxiii, 1, 1887. PFLÜGER.—Internat. Ophth. Congress, Milan, 1880. WAHLFORS.—B. d. o. G., 1888.

During an experiment with either of the forms of apparatus described the column of mercury in the manometer or the air-bubble in the capillary tube often shows movements which are synchronous with the pulse and respirations. These were observed by C. Weber, who made the first manometric experiments on the eye under Ludwig. In graphic records they may be as distinct as the pulse and respiratory waves on an ordinary blood-pressure curve. They may be superposed upon even larger waves which follow the curve of Traube-Hering waves upon the blood-pressure curve.

When the pulsations are evident they afford a sure indication that there is free communication between the eye and the manometer.   On
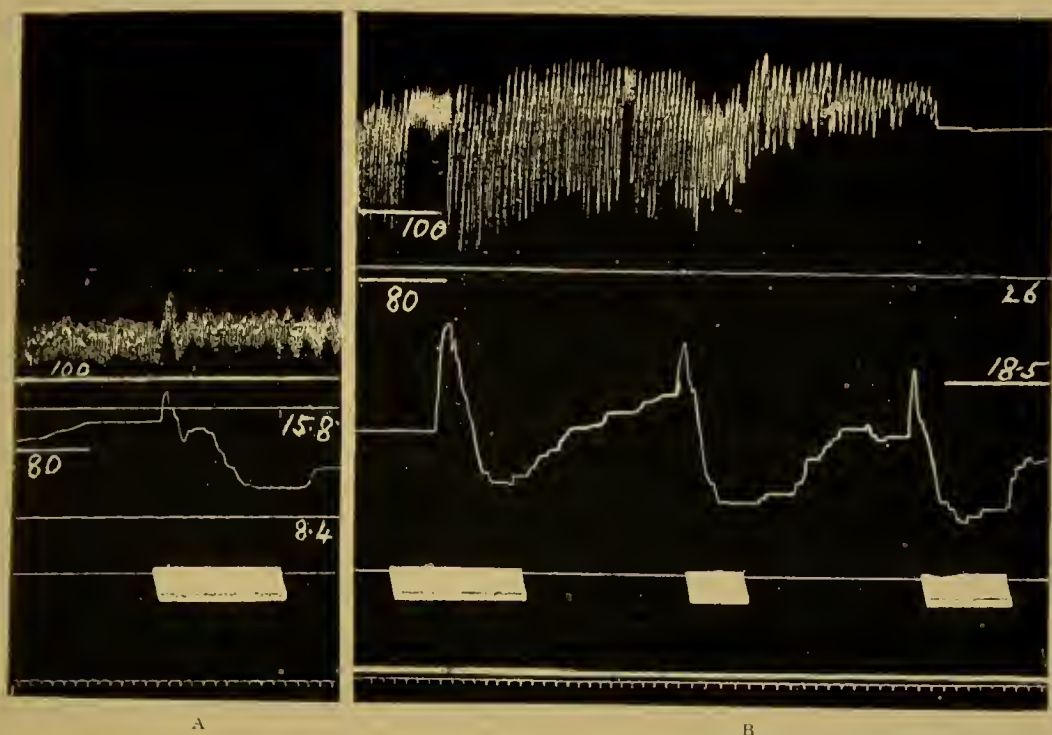
FIG. 707.—STIMULATION OF THE CERVICAL SYMPATHETIC.

Henderson and Starling, Jl. of Physiology, xxxi. A. Stimulation of the sympathetic nerve in a cat. Blood-pressure measured in aorta, intra-ocular pressure in right eye. Both vagi have been cut, and the right sympathetic stimulated. B. Stimulation of the sympathetic nerve in a dog. In this experiment the stimulus was applied to the annulus of Vieussens. It is repeated three times with similar effect. The sudden rise of pressure is due to contraction of the orbital muscle, the slow fall to constriction of the intra-ocular vessels.

the other hand, their absence does not necessarily denote that the cannula is blocked. They are absent when the blood-pressure is low— e. g. when the heart is failing (Höltzke, v. Schultén, Bellarminoff, Stocker); and Koster and Leber noticed that with a mercury manometer of fine lumen (1 sq. mm. diameter) they are scarcely visible. The latter investigator, indeed, found that they were most obvious with a wide bore manometer. Bellarminoff, and Hess and Heine found them only clearly visible with slightly raised intra-ocular pressures. The conditions are, indeed, almost exactly those which obtain in the cranial cavity, the eye being for the pressures under consideration a

closed rigid box. It is true that the pulsations of individual retinal arteries are visible ophthalmoscopically only under abnormal conditions, but even then the summation of the effects of all the intra-ocular arteries, communicated as they are to the inelastic intra-ocular fluids, produce a result which is not negligible. They are very well demonstrated with the micromanometer (Donders), especially on non-narcotised rabbits (Leber).

These pulsations have been observed clinically in cases where part of the wall of the globe is pathologically thinned, as in keratoconus (q. v., Javal, Gullstrand, Wagenmann, Callies, Preller), or where there is a minute perforation, such as a perforated corneal ulcer or scleral wound (Förster, v. Michel). The change in corneal curvature in conical cornea during the pulsations has been carefully observed by Wagenmann and Gullstrand. It would appear that in Wagenmann's case the peripheral parts of the cornea became more curved, whilst in Gullstrand's the apex became more curved and the periphery flatter.

HESS AND HEINE.—A. f. O., xlvi, 2, 1898. DONDERS.—A. f. O., xvii, 1, 1871. FÖRSTER.— K. M. f. A., ii, 1864. v. MICHEL.—Sitzungsbericht d. phys.-med. Ges. zu Würzburg, 1881.
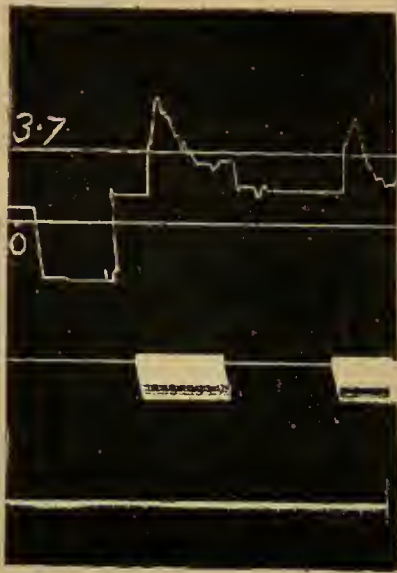
FIG. 708.—STIMULATION OF THE CERVICAL SYMPATHETIC.

Henderson and Starling, Jl. of Physiology, xxxi. This is taken from the same animal immediately after it had been bled to death and the blood-pressure had fallen to zero. The stimulus, as in the last figure, was applied to the annulus of Vieussens.

Any external pressure upon the eye will naturally raise the internal pressure temporarily. This is shown by pressure with the finger or a bandage, action of the extrinsic muscles, etc. Owing to this action of the extrinsic muscles it is necessary in manometric observations to curarise the animal. Even this procedure does not eliminate the action of the unstriated muscles in the orbit, and these are particularly well developed in cats, dogs, etc. I was able to show that the rise in pressure caused by stimulation of the cervical sympathetic and described by Adamük, v. Hippel and Grünhagen, and others was due to contraction of the unstriped muscle contained in the orbit, since it occurs for a considerable time after the death of the curarised animal. This result was confirmed by Henderson and Starling (Figs. 707–708).

Prolonged pressure externally gradually squeezes out fluid from the eye, so that the pressure again becomes normal, but on removing the external pressure the tension remains subnormal until increased secretion produces compensation—a comparatively slow process. Hence, after prolonged use of a pressure-bandage the intra-ocular pressure may remain subnormal for some time.

Much attention has been paid to the problem whether the pressure in the anterior chamber is equal to that in the vitreous. Theoretical

considerations would lead one to expect, *à priori*, that there might be some difference, borne by the tension of the lens diaphragm—*i. e.* the lens and its suspensory ligament. This was the more probable in the days when the zonule of Zinn was held to be a definite membrane. Now that it is known that filtration takes place with the greatest ease through the suspensory ligament and that the lens is comparatively mobile owing to the extensibility of the zonule, it is obvious that any difference of pressure must be very slight. This is confirmed by direct observation.

Monnik first showed in freshly excised eyes that when fluid was forced in the pressure rose *pari passu* in both chambers, until very high pressures were employed, when the difference amounted to only 1—3 mm. Hg. Priestley Smith showed that under similar circumstances a very slightly greater pressure in the vitreous—about 1 mm. Hg.—caused almost complete abolition of the anterior chamber.

Experiments on living animals have led to confirmatory results (Adamük, Schöler, v. Schultén, Höltzke, Bödeker). Bellarminoff found the pressure in the vitreous the same as the pressure in the anterior chamber of the opposite eye of the same animal simultaneously observed. Hamburger observed the pressures in the anterior chamber and vitreous of the same eye with the differential manometer; there was no movement of the level of contract of the water and petroleum in the instrument such as would have occurred had the pressures been unequal.

That there is a minute difference in pressure between the fluid in the posterior and anterior chambers follows from the fact that the lymph is gradually displaced forwards to its exit at the filtration angle. The difference is so slight, however, that it is less than the unavoidable errors of manometric experiment.

A cognate question is the effect of activity of the iris or ciliary muscle upon the intra-ocular pressure. Experiments on excised eyes before the loss of excitability of the muscles show that this produces no change in pressure, and this is confirmed by stimulation of the ciliary ganglion, etc., in curarised animals (Grünhagen, Völckers and Hensen, Adamük, Hess and Heine). During accommodation the suspensory ligament is relaxed, so that the lens sinks slightly and can be made to tremble (Coccius, Hess); this affords very delicate evidence of the absence of any difference in pressure. Further, Helmholtz showed that owing to the incompressibility of the aqueous the forward movement of the anterior pole of the lens during accommodation must be compensated for by the retraction of the iris periphery and deepening of the anterior chamber in this situation.

The suggestion that any increase in pressure in the vitreous due to the action of the ciliary muscle might be compensated for by pressure of blood out of the eye has been negatived by Grönholm, who stimulated the ciliary region in cats and rabbits after bleeding to death. Since these animals have very limited powers of accommodation Hess considered it advisable to investigate monkeys and pigeons, which have a range of accommodation of 10—12 D; he obtained the same negative result.

The results obtained with eserin and atropin have been more equivocal (*v. infra*).

MONNIK.—A. f. O., xvi, 1, 1870. PRIESTLEY SMITH.—Ophth. Rev., vii, 1888; Glaucoma, London, 1891. GRÜNHAGEN.—Berliner klin. Woch., 1866. HENSEN AND VÖLCKERS. —C. f. d. med Wiss., 1856; Experimentaluntersuchung ü. d. Mechanismus d. Akkommodation, Kiel, 1868. ADAMÜK.—C. f. d. med. Wiss., 1867. HESS.—A. f. O., xliii, 3, 1897. HESS AND HEINE.—A. f. O., xlvi, 2, 1898. COCCIUS.—Der Mechanismus d. Akkommodation d. menschl. Auges, Leipzig, 1868. HESS.—A. f. O., xlii, 1, 1896. v. HELMHOLTZ.—A. f. O., i, 2, 1855. GRÖNHOLM.—A. f. O., xlix, 3, 1901.
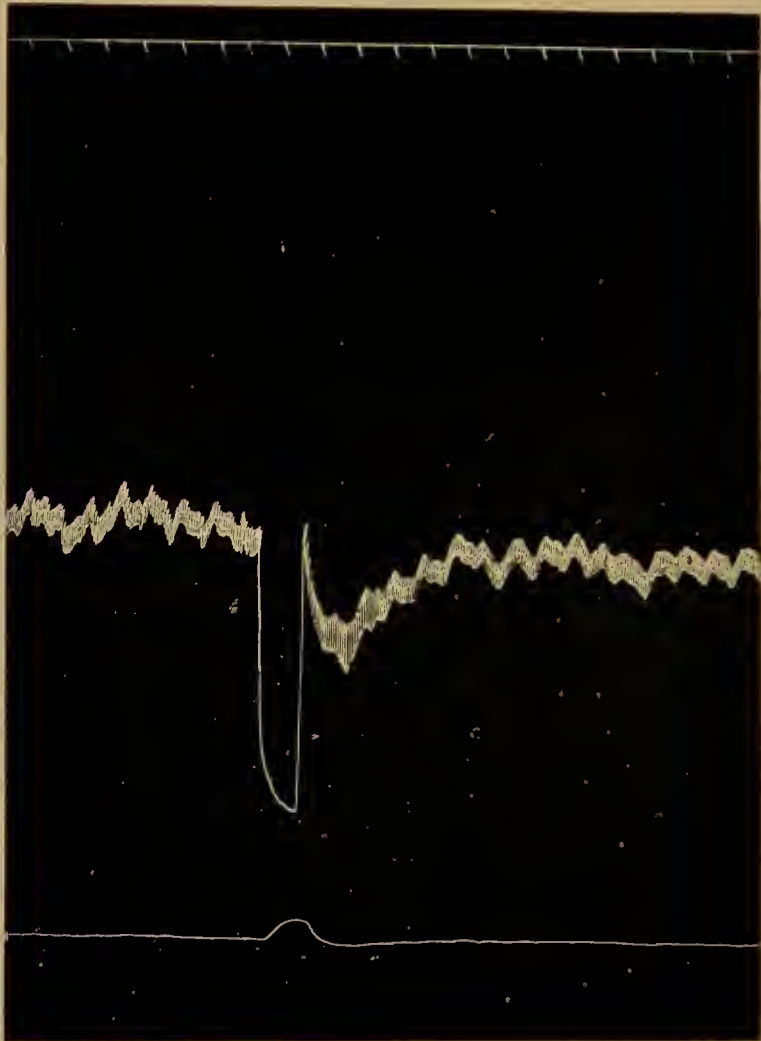
FIG. 709.—COMPRESSION OF THE THORACIC AORTA.

Parsons, The Ocular Circulation. Dog. Morphia, A.C.E., and curare. Femoral blood-pressure; cannula in a.c. Compression of thoracic aorta. Time in 10-second intervals.

It has already been emphasised that the production of the intra-ocular fluid is compatible with the theory that it is a filtration product from the blood. It has been shown that the lymph escapes from the eye for the most part at the angle of the anterior chamber. Under normal conditions the rates of inflow and outflow are approximately
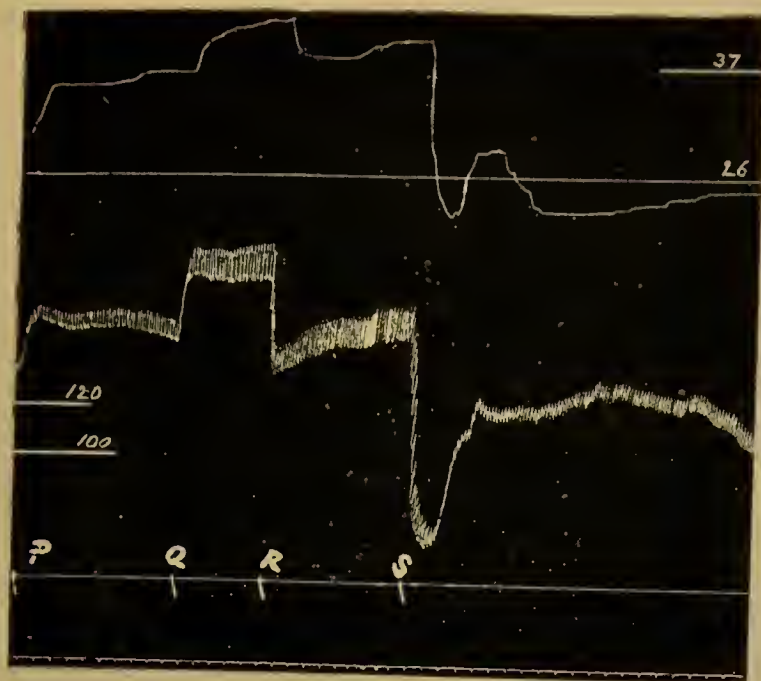
FIG. 710.—COMPRESSION OF AORTA, ETC.

Henderson and Starling, Jl. of Physiology, xxxi. To illustrate the effects of mechanical interference with the circulation in a dog. Blood-pressure measured in left carotid, intra-ocular pressure in right eye. From P to S the aorta was occluded. From Q to R the right vertebral and subclavian were also occluded. In this, as in all the tracings, the scale to the right indicates the intra-ocular pressure reduced to millimetres of mercury. Time marker 10 seconds intervals.
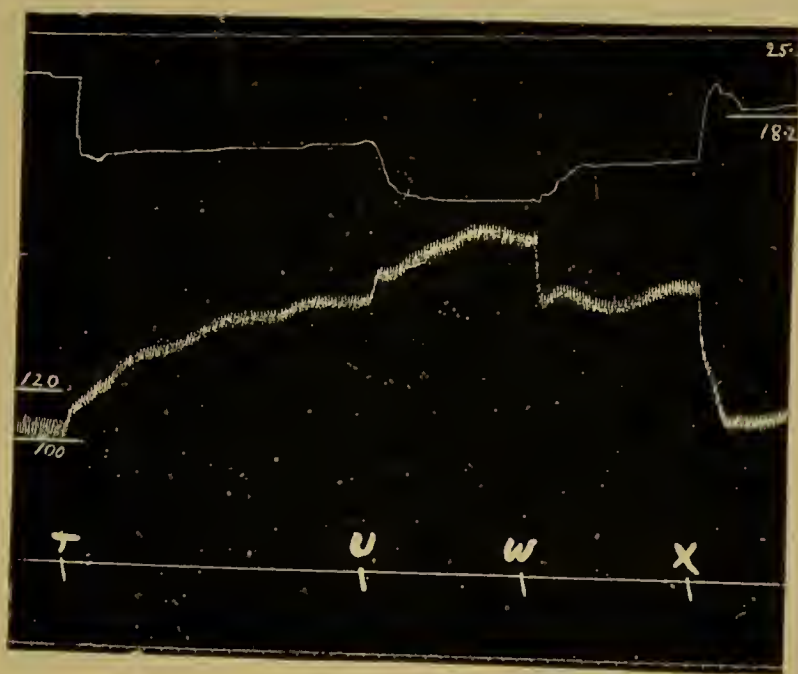
FIG. 711.—COMPRESSION OF CAROTID, ETC.

Henderson and Starling, Jl. of Physiology, xxxi. Dog. Blood-pressure in left carotid, intra-ocular pressure in right eye. From T to X occlusion of right carotid, from U to W occlusion of right vertebral and subclavian.

equal, so that the pressure inside the eye is kept almost constant, the variations being slight. It has further been shown that this mean pressure is about 25 mm. Hg. above the surrounding atmospheric pressure. Under these circumstances, the absence of any "vital" secretory mechanism being admitted, it is obvious that the source of energy of the constant raised pressure must be derived from the blood-pressure. Experiment shows, indeed, that the relationship is extremely intimate, the curve of intra-ocular pressure following that of the blood-
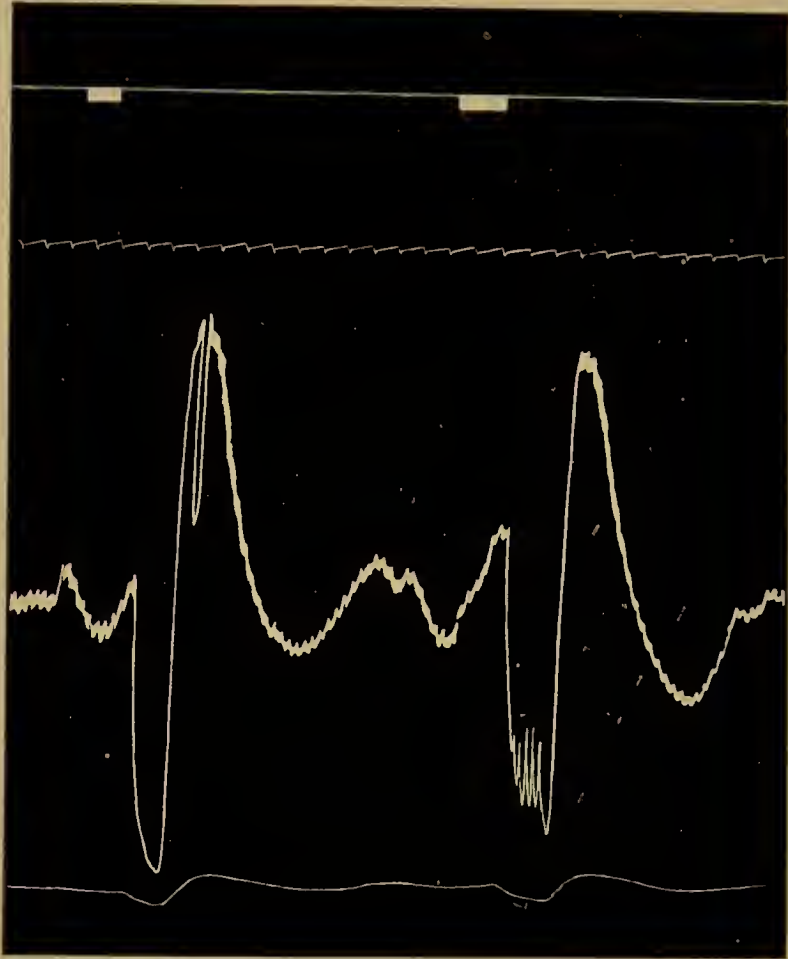
FIG. 712.—STIMULATION OF PERIPHERAL END OF VAGUS.

Parsons, The Ocular Circulation. Dog. Intra-cranial pressure raised to 135 mm. Hg. by injection of normal saline into the skull through a pressure-gauge inserted in the parietal region. Both vagi cut. Stimulation of peripheral end of right vagus.

pressure very exactly. This is a passive response, due, as in other parts of the body, of which innumerable examples might be given, to the overwhelming effect of the rise or fall of blood-pressure produced by widespread vaso-constriction or dilatation in other areas, particularly in the great vascular reservoir, the splanchnic area; vaso-constriction in the splanchnic area, for example, leads to so large a rise of blood-pressure that any attempt at vaso-constriction in the ocular area is overcome, the arterioles are burst open, and passive dilatation with consequent increased transudation of lymph and rise of intra-ocular pressure occurs.

The delicacy of the response has already been shown in the representation of the cardiac and respiratory oscillations in the manometer or air-bubble. The passive effect of larger changes is clearly shown by the reproduction of the general curve of the blood-pressure. The intra-ocular curve is slightly delayed and flatter, owing to the inertia of the eye, which acts like a natural plethysmograph.
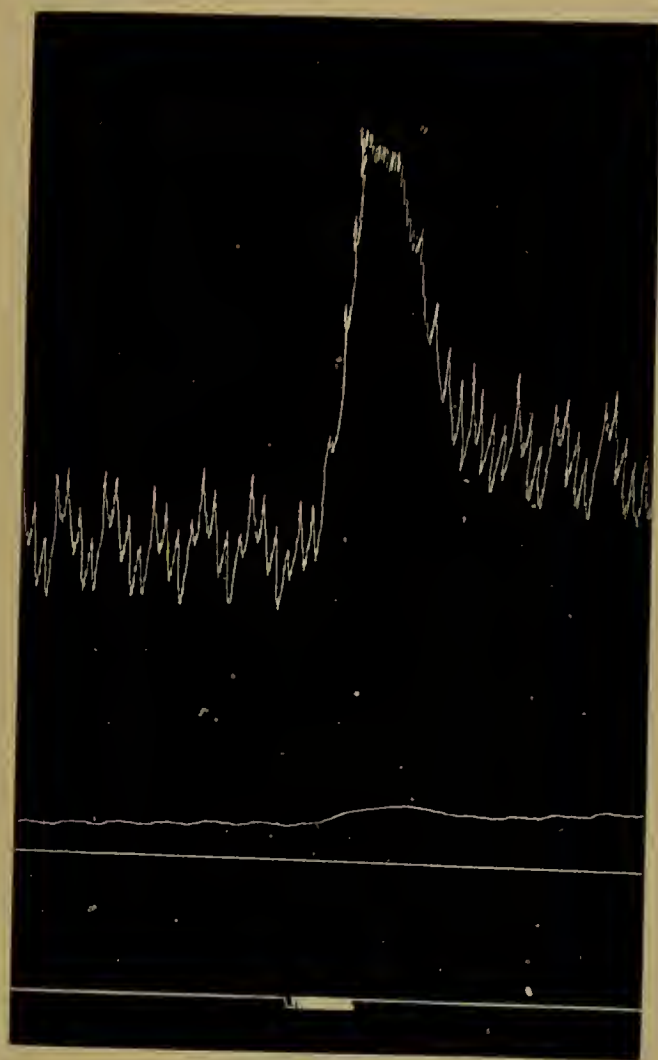
FIG. 713.—STIMULATION OF VASOMOTOR CENTRE.
Parsons, The Ocular Circulation. Dog. Morphia, A.C.E., and curare. Right carotid blood-pressure; left intra-ocular pressure in a.c. Traube-Hering curves; stimulation of vaso-motor centre.

The general blood-pressure may be varied by many means: (1) mechanical; (2) stimulation, etc., of nerves or parts of the central nervous system; (3) asphyxia; (4) drugs; (5) bleeding or injection of fluids; (6) death. The local blood-pressure may be conceivably under the control of the nervous system as in other areas of the body—i. e. there may be vaso-constrictor and vaso-dilator nerves; it may be further influenced by blockage, pathological or experimental, of the venous outflow.

Mechanical alterations in the general blood-pressure may be produced by ligature of the aorta or other arteries. The effect of ligature of the carotid of the same side as the eye under observation must first receive attention. Tonometric observations of digital compression of the carotid in man tend to show a slight fall in pressure (2—2·5 mm. Hg., Golowin). In experimental observations on lower animals the double —intra- and extra-cranial—blood-supply must be taken into account (*v.* p. 940). Adamük found in cats and dogs a fall of 6—8 mm. Hg., Graser of 5—6 mm. Hg. ; v. Schultén in rabbits 8—15 mm. Hg., Heine 1—2 mm. Hg. When the external carotid is tied I have found compression of the common carotid produce very little effect. The smallness of the effect which has been observed is due to the free anastomosis in the circle of Willis.

Compression of the abdominal or thoracic aorta causes a large rise in blood-pressure in the upper part of the body. This is accompanied by a large rise in the intra-ocular pressure (Fig. 709) —v. Hippel and Grünhagen, 30—50 mm. Hg.; v. Schultén, 20—34 mm. Hg. ; Henderson and Starling, about 10 mm. Hg. Further occlusion of the vertebral and subclavian arteries increases the effect (Figs. 710, 711).

GOLOWIN.—In Nagel's Jahresbericht, 1901.

FIG. 714.—STIMULATION OF SPLANCHNIC NERVES.

Henderson and Starling, Jl. of Physiology, xxxi. Effect of stimulation of splanchnic nerves in a dog. Blood-pressure measured in femoral artery, intra-ocular pressure in right eye.

Stimulation, etc., of nerves.—The general blood-pressure may be influenced through nervous paths in various manners : (1) by stimulation of the cardio-inhibitory nerves—*i. e.* the peripheral end of the vagus ; (2) by acting upon the vasomotor mechanism of the peripheral arterioles—(*a*) by cutting off the tonic vaso-constrictor impulses from the vasomotor centre, as by section of the spinal cord ; (*b*) by stimulating the vasomotor centre in the medulla oblongata : (*c*) by exciting or depressing the vasomotor centre indirectly by stimulation of the central ends of sensory nerves or depressor nerves.

Stimulation of the peripheral end of the vagus causes cardiac inhibition and consequent sudden fall of blood-pressure. The intra-ocular pressure shows a similar fall, amounting to about 10—12 mm. Hg. (Adamük, Schöler, v. Schultén, Parsons) (Fig. 712).

Section of the spinal cord high up—*c. g.* in the upper cervical region— cuts off the tonic vaso-constrictor impulses descending the cord from the medullary vasomotor centre. The arterioles of large areas of the body, but especially of the splanchnic area become dilated, so that the general blood-pressure falls. This is accompanied by a similar fall in intra-ocular pressure amounting to 10—15 mm. Hg. (v. Hippel and Grünhagen, Parsons).

Stimulation of the vasomotor centre in the medulla causes a large rise in blood-pressure, which is accompanied by a corresponding rise in intra-ocular pressure (v. Hippel and Grünhagen, Parsons) (Fig. 713). v. Hippel and Grünhagen attributed part of the rise to stimulation of the fifth nerve nucleus. This may be considered disproved, the rise being entirely due to constriction of arterioles, especially those of the splanchnic area in the abdomen. Stimulation of the peripheral cut end of the spinal cord or splanchnic nerves produces the same result through the same mechanism (v. Hippel and Grünhagen, v. Schultén, Parsons, Henderson and Starling) (Fig. 714).

Stimulation of the central end of sensory or mixed nerves—e. g. the
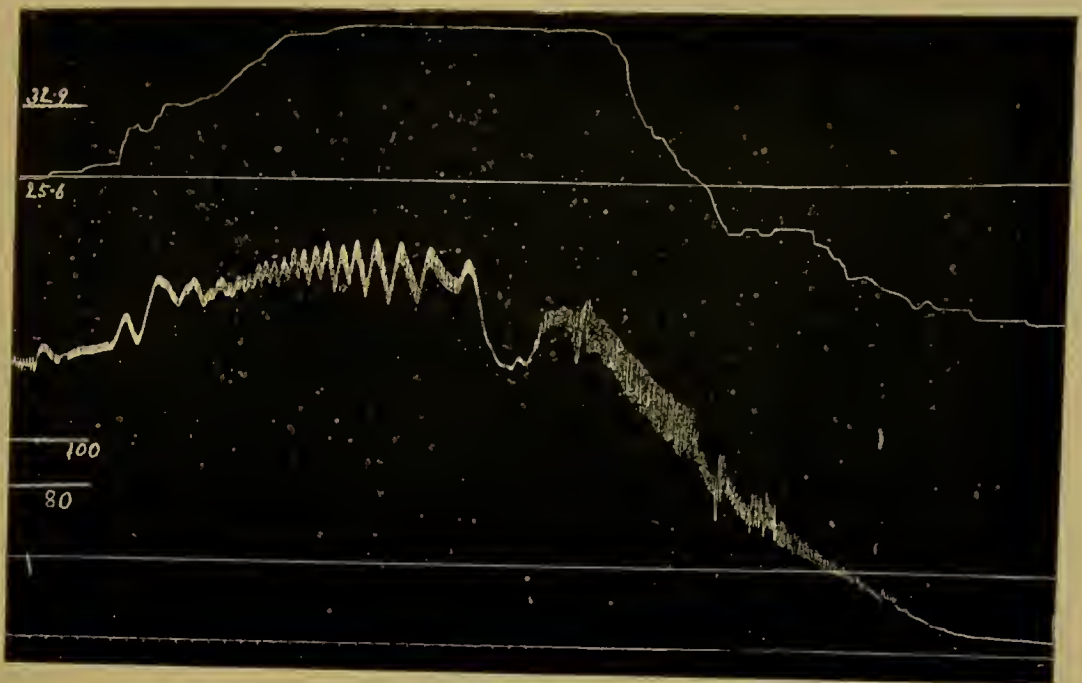
FIG. 715.—ASPHYXIA.

Henderson and Starling, Jl. of Physiology, xxxi. Asphyxia in dog. Left carotid blood-pressure; right intra-ocular pressure in a.c.

sciatic—causes rise of blood-pressure through the vasomotor centre and coincident rise of intra-ocular tension. The same occurs when the central end of the fifth nerve is stimulated; this is the explanation of the rise in intra-ocular pressure which occurs when nicotin is applied to the cornea, as in v. Hippel and Grünhagen's experiments.

Stimulation of the central end of the depressor nerve in the rabbit causes fall in general blood-pressure and in intra-ocular pressure. In other animals the depressor fibres run in the vagus trunk, so that stimulation of the central end of the vagus may produce either a pressor effect, as with most sensory nerves, or a depressor effect. Depressor fibres are often present in other sensory nerves, so that a depressor effect may be occasionally obtained from them; in any case the intra-ocular pressure follows the blood-pressure.

Asphyxia.—The rise in blood-pressure due to stimulation of the vasomotor centre by the altered constituents of the blood during the first stage of asphyxia is accompanied by a corresponding rise in the intra-ocular tension (Adamük, v. Hippel and Grünhagen, Parsons, Henderson and Starling). If air is admitted into the lungs again at this stage, the intra-ocular curve follows the blood-pressure curve. If the asphyxia is continued the intra-ocular pressure generally falls *pari passu* with the general blood-pressure (Parsons, Henderson and Starling) (Fig. 715). I occasionally found the intra-ocular pressure to continue to rise, and I attributed this to the obstruction to the return of venous blood to the over-charged right heart at this stage. It is more probably due to an experimental error (*cf.* Henderson and Starling), but it is interesting to note that Schöler usually found a fall of intra-ocular tension during asphyxia. It is not improbable that the results may vary with the condition of the animal.

Drugs.—The same passive rise or fall of intra-ocular pressure, according to the effect upon the blood-pressure, is seen when drugs are injected into the circulation. The effects of anæsthetics account for some of the variations in the records of the mean normal tension (*v.* p. 1054). Adrenalin, nicotin (Fig. 716), pilocarpin, quinine, amyl nitrite, and large doses of chloroform give results in accordance with their effects upon the blood-pressure. It may be noted that pilocarpin shows no specific secretory effect. Nicotin and adrenalin have also a local vasomotor action, which will be considered later (*v. infra*).

FIG. 716.—INJECTION OF NICOTIN.
Parsons, The Ocular Circulation. Dog. Morphia, A.C.E., and curare. Femoral blood-pressure; external carotid tied. One minim of 5 per cent. solution of nicotin injected into femoral vein. Time in 10-second intervals.

Bleeding or injection of fluids.—Troncoso found that injection of

large quantities of normal saline solution into the circulation caused a large but transitory rise in intra-ocular pressure. His experiments are of little value, since the blood-pressure was not simultaneously observed. It would be interesting to observe the effects of the injection of so-called lymphogogues upon the intra-ocular pressure, but no investigations have as yet been published. Heine found that if the blood-pressure in rabbits is greatly raised by the injection of fluid the intra-ocular tension shows a parallel rise; thus, with a blood-pressure of 300 mm. Hg. the intra-ocular pressure was 100 mm. Hg.

Bleeding produces no effect until the blood-pressure begins to fall (v. Schultén). Leber found that on bleeding to death the ocular pressure in the rabbit rapidly fell from 18·5 mm. Hg. to 9 mm. Hg.

TRONCOSO.—La Clinique opht., vii, 1901; Ann. d'Oc., cxxvi, 1901.

Death.—At death the intra-ocular pressure falls rapidly to about 10 mm. Hg. It then gradually and very slowly continues to fall, owing to the filtration of the aqueous, until it reaches zero.

Vasomotor nerves.—There is no doubt that the iris possesses vasomotor nerves, and that the vaso-constrictor fibres run in the cervical sympathetic.[1] Ophthalmoscopic observations upon men and animals render it probable that the retinal and choroidal (as observed in albinos) vessels are also subject to nervous control. This method, as applied to animals, is open to grave doubt, as it is almost impossible to be certain of such minute changes, especially when the optical conditions and the bias of preconceived ideas are taken into consideration.

It may be definitely stated that the presence of vaso-constrictor fibres to the intra-ocular vessels has been proved by the manometric method (Parsons, Henderson and Starling), but that the question of vaso-dilators is still *sub judice*.

Reviewing first the observations of the early experimenters, it was found in cats that stimulation of the cervical sympathetic caused a rise

FIG. 717.—VASO-CONSTRICTOR NERVES.

Parsons, The Ocular Circulation. Dog. Morphia, A.C.E., and curare. Femoral blood-pressure; cannula in anterior chamber. Stimulation of superior cervical ganglion. From above down: signal, time in 10-second intervals, blood-pressure, intra-ocular pressure.

[1] *See* PARSONS, 'The Neurology of Vision,' London, 1904.

in intra-ocular pressure of about 5 mm. Hg. (Adamük, v. Hippel and Grünhagen, Höltzke and Graser, Bellarminoff). v. Schultén obtained the same result in dogs. Experiments on rabbits gave less concordant results (Wegner, Neuschüler, etc.)

Section of the cervical sympathetic in cats and dogs gave a fall of about 6 mm. Hg. (Adamük, Höltzke, Graser, Lagrange and Pachon); v. Hippel and Grünhagen failed to obtain this result.

Extirpation of the superior cervical ganglion in dogs gave a fall of pressure of 6 mm. Hg. as estimated by Fick's tonometer (Lagrange and Pachon). The hypotony lasted well marked for four weeks, was less in six weeks, and had disappeared in eight weeks. The same operation in man has been stated to produce a like result. Schmidt-Rimpler found that the low tension lasted five months. Abadie, Jaboulay, and other surgeons have obtained equivocal results. Jonnesco and Floresco obtained very
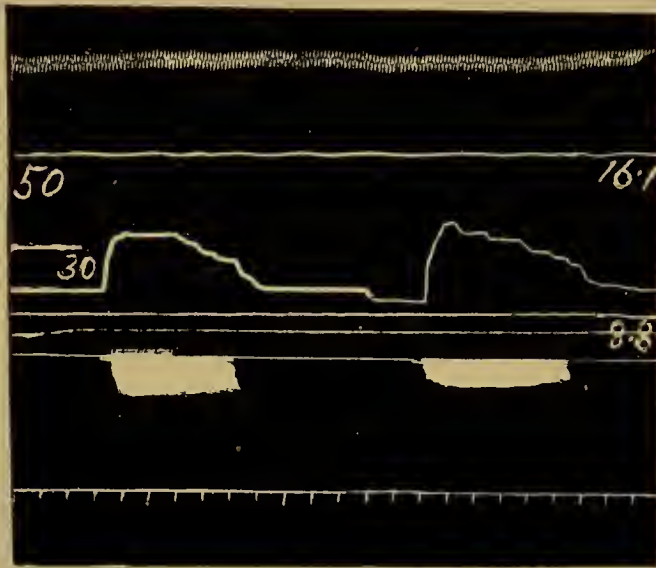
FIG. 718.—STIMULATION OF THE GASSERIAN GANGLION.
Henderson and Starling, Jl. of Physiology, xxxi. Cat. Stimulation of the Gasserian ganglion after section of the root of the fifth.

striking results. The operation, which was first employed for epilepsy and exophthalmic goitre, and later for glaucoma, was founded upon faulty observations and has fallen into well-deserved disrepute.

The rise in intra-ocular pressure which occurs when the peripheral end of the cervical sympathetic is stimulated in lower animals is due to the contraction of unstriped muscle in the orbit, thus producing external pressure upon the globe (v. Hippel and Grünhagen, Parsons, Henderson and Starling). It has, however, been possible to obtain a definite fall in the intra-ocular pressure when the nerve is stimulated. Any action of the external muscles is, therefore, more than compensated for, and the effect must be due to contraction of the intra-ocular blood-vessels. Moreover, the contraction of the vessels comes on more slowly than the contraction of the orbital muscles and retraction of the nictitating membrane (cf. Langley and Anderson on the iris).[1] On stopping

[1] LANGLEY AND ANDERSON, 'Journ. of Physiology,' xiii, 1892.

stimulation the vessels slowly dilate again, and with the dilatation the intra-ocular pressure returns to normal.

Stimulation of the fifth nerve or of the Gasserian ganglion is acknowledged by all observers to cause rise in the intra-ocular pressure. This has been attributed to the action of vaso-dilator fibres. In most cases the excitation is accompanied by a considerable rise in blood-pressure, so that the effect may more probably be attributed to the passive dilatation. Bellarminoff obtained different results from different parts of the Gasserian ganglion, but when one considers the great difficulty of preventing a spread of current in this situation the results require confirmation. The experimental difficulties are considerable, but Henderson and Starling succeeded in overcoming them. The Gasserian ganglion is most accessible in cats. If the fifth nerve is efficiently divided proximal to the ganglion, stimulation causes no change in blood-pressure and the ocular pressure rises. This rise, however, is accompanied by retraction of the nictitating membrane and is due to stimulation of the sympathetic fibres from the cervical sympathetic which pass over the ganglion. These observers therefore removed the superior cervical ganglion in three cats and allowed the post-ganglionic fibres to degenerate. It was then found that stimulation of the Gasserian ganglion caused no change in intra-ocular pressure. Henderson and Starling conclude that the fifth nerve contains no secretory or vaso-dilator fibres to the eye.
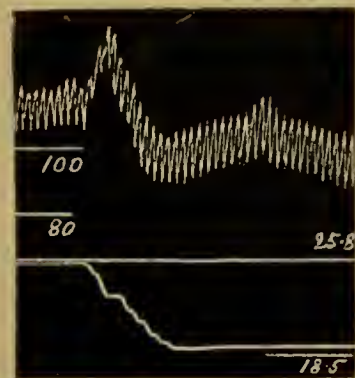
FIG. 719.—INJECTION OF ADRENALIN.

Henderson and Starling, Jl. of Physiology, xxxi. At the spot marked on the intra-ocular pressure line 0·118 c.c. of a 0·1 per cent. adrenalin solution was injected into the femoral vein. The superior cervical ganglion had been removed immediately prior to the observation.

Confirmatory evidence as to the vaso-motor supply of the eye is obtained from the action of adrenalin and nicotin. It is known that both of these drugs act upon the walls of the blood-vessels, causing constriction; nicotin has a further and much more marked effect upon the sympathetic ganglia. By injecting adrenalin into the carotid artery I was able to demonstrate a distinct fall in the intra-ocular pressure before the passive rise due to the rise in blood-pressure caused by the action of the drug upon the body vessels. I failed to obtain a like result with nicotin, but Henderson and Starling, by using smaller doses, have been more fortunate. Four experiments were made on intact animals; of these, in two the local effect predominated with both adrenalin and nicotin, the blood-pressure rising whilst the intra-ocular pressure fell; in one the two effects nearly counterbalanced one another; in the fourth the intra-ocular rise appeared to be entirely passive. In three cats the superior cervical ganglion had been removed immediately before the experiment. In one a purely passive effect occurred in both eyes. In the remaining two the local effect to adrenalin was extremely well marked. Nicotin, on the contrary, showed no local effect on the eye of the side on which the superior cervical

ganglion had been excised. On the other eye a similar dose, though causing a considerable rise of blood-pressure, was practically without effect upon the intra-ocular pressure. In a fourth cat, in which the superior cervical ganglion had been removed and time allowed for degeneration, the rise in blood-pressure which in each case followed the administration of the two drugs in question was followed by a purely passive rise of intra-ocular pressure. The effects of adrenalin and nicotin therefore vary according to the preponderance of the local or general effect upon the blood-vessels.

HERTEL.—A. f. O., xlix, 2, 1899. NEUSCHÜLER.—Ann. di Ott., xxviii, 1899. ABADIE. —A. d'O., xix, 1899. LAGRANGE AND PACHON.—Comptes rendus de la Soc. de Biol., 1900. SCHMIDT-RIMPLER.—B. d. o. G., 1900. JONNESCO AND FLORESCO.—Jl. de Phys., iv, 1902.

The intra-capillary—and therefore the intra-ocular—pressure is dependent, not only upon the arterial pressure and the size of lumen
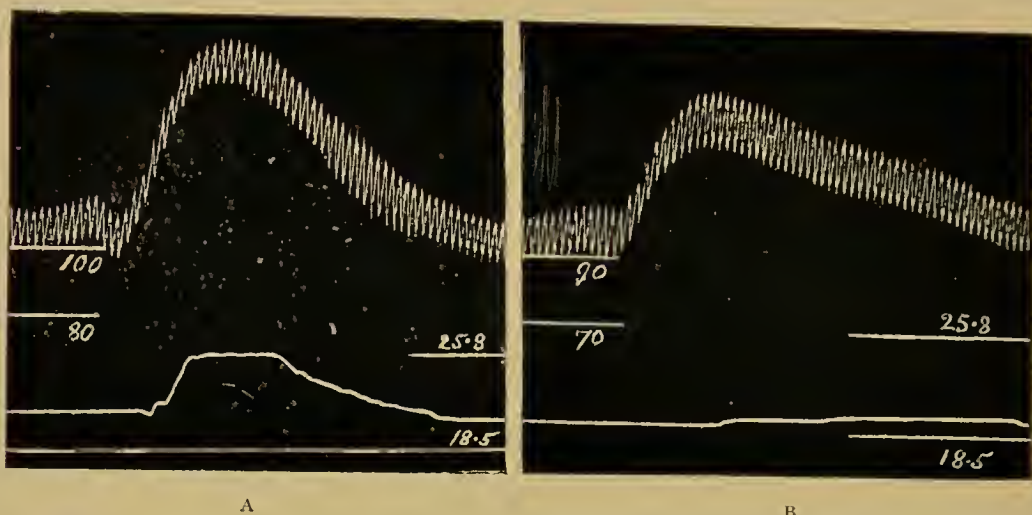
FIG. 720.—INJECTION OF NICOTIN.

Henderson and Starling. Jl. of Physiology, xxxi. A. The same eye of the same cat as in the last tracing being still used for the measurement of the intra-ocular pressure, 0·118 c.c. of a 2 per cent. solution of nicotin was injected into the femoral vein at the place marked on the intra-ocular pressure tracing. B. The opposite eye of the same cat was now employed. On this side the sympathetic was intact. At the place marked on the intra-ocular pressure curve 0·118 c.c. of the same nicotin solution was again injected, the effect of adrenalin remained exactly as in Fig. 719, and is therefore not reproduced.

of the arterioles, but also upon the freedom of outflow of the venous blood. Rise in general venous pressure is probably in all cases more than counteracted by the accompanying fall in arterial pressure. When, however, there is some obstruction to the venous return near the eye the intra-ocular pressure rises. Adamük, Graser, and v. Schultén describe slight and not very constant increase of pressure when the external and internal jugular veins are tied. It is not surprising that this produces little result when one remembers the extremely free anastomosis of the veins and the thinness of their walls, which permits the accommodation of a considerable excess of blood without much altering the venous pressure. Memorsky could not observe any definite dilatation of the intra-ocular veins under these circumstances.

Ligature of the venæ vorticosæ, on the other hand, produces a very large rise of intra-ocular pressure, amounting in cats to 90 mm. Hg. (Adamük). In rabbits Leber obtained double the normal pressure and more. Koster Gzn found the maximum rise, when all four vertex veins were tied, to be about 70 mm. Hg.; the rise is much less marked if only three or two veins are ligated. In albinos a local hyperæmia of the iris and ciliary body is seen; this is limited when only one vein is tied to the corresponding quadrant. The rise in tension is due primarily to the dilatation of the vessels, and secondarily to the high capillary pressure inducing increased transudation. The anterior chamber becomes shallow, and the filtration of fluid from the eye is thereby at first diminished, so that increased production is accompanied by diminished excretion. The extreme congestion leads to the transudation of highly albuminous lymph; opacities appear in the vitreous and degenerative changes—cataract—in the lens. The maximum tension is not long maintained; it diminishes gradually during the first day, and in the course of weeks returns to the normal, probably owing to the opening up of anastomoses (Ad. Weber, Koster).

ADAMÜK.—C. f. d. med. Wiss., 1866; Ann. d'Oc., lviii, 1867. GRASER.—Dissertation, Erlangen, 1883. v. SCHULTÉN.—A. f. O., xxx, 3, 1884. LEBER.—A. f. O., xix, 2, 1873. KOSTER GZN.—A. f. O., xli, 2, 1895. AD. WEBER.—A. f. O., xxii, 4, 1876.

Much attention has been directed to the effect of mydriatics and miotics upon the intra-ocular pressure. Early observers found that atropin caused a slight fall in pressure (Wegner, Adamük, Leber); Adamük elsewhere describes diminution in the rapidity of excretion of aqueous. Tonometric observations on man confirmed the diminution in tension (Ad. Weber, Dor, Pflüger). Later observers obtained discordant results with the manometer. Thus, Pflüger and Stocker obtained diminution, Höltzke and Graser increase, and Bellarminoff no difference in the intra-ocular pressure. It must be concluded that under normal pressures the effect of atropin is negligible. There is no doubt that with abnormally raised tensions, such as are met with in glaucoma, atropin distinctly raises the pressure owing to mechanical blocking of the filtration angle by the dilated pupil (see also p. 984).

Local application of cocain was found by Stocker to cause slight rise of pressure, followed by a fall of 2—3 mm. Hg. This is probably due to local constriction of the vessels. Vollert obtained similar results with eucain. Subconjunctival injection of suprarenin causes dilatation of the pupil and constriction of the vessels, accompanied by fall of pressure (Wessely). Clinically, local application of adrenalin has in rare cases been found to cause rise of tension, probably owing to the pathological condition of the eye and induced by the dilatation of the iris (MacCallan). Absorption into the general circulation would tend to cause a passive rise of tension due to the rise in general blood-pressure (v. p. 1064).

Miotics have generally been found in normal eyes to produce a slight rise in pressure, coming on before the constriction of the pupil, followed by a fall; this applies to both eserin and pilocarpin (Höltzke and Graser, Stocker, Grönholm, Schlegel, Golowin). The primary rise

in pressure is difficult to explain; it is probably within the range of experimental error. The secondary fall is due to the constriction of the pupil, which opens up the filtration angle, and accords with the well-known results upon glaucomatous eyes (v. p. 984). Of interest in this connection is the increase in corneal curvature observed on instillation of eserin (v. Reuss).

No part of the action of mydriatics and miotics can be attributed to their effects upon the ciliary muscle, as has been already shown.

WEGNER.—A. f. O., xii, 2, 1866. ADAMÜK.—C. f. d. med. Wiss., 1866; Ann. d'Oc., lxiii, 1870. LEBER.—In G.-S., ii, 1876; ii, 2, 1903. AD. WEBER.—A. f. O., xiii, 1, 1867. DOR.—A. f. O., xiv, 1, 1868. PFLÜGER.—A. f. A., ii, 1872; Internat. Ophth. Congress, 1880; B. d. o. G., 1882. STOCKER.—A. f. O., xxxiii, 1, 1887. HÖLTZKE.—A. f. O., xxix, 2, 1883. GRASER.—Dissertation, Erlangen, 1883. BELLARMINOFF.—Pflüger's Archiv, xxxix, 1886. VOLLERT.—Münchener med. Woch., 1896. WESSELY.—B. d. o. G., 1900. MacCAL-LAN.—T. O. S., xxiii, 1903. GRÖNHOLM.—A. f. O., xlix, 3, 1900. SCHLEGEL.—Arch. f. exp. Path. u. Pharm., xx, 1886. GOLOWIN.—In Nagel's Jahresbericht, 1895. v. REUSS.—A. f. O., xxiii, 3, 1877.

CHAPTER XXI

GLAUCOMA

HIPPOCRATES is the first author in whose writings the word γλαυκός is used in reference to the diseases of the eye ; he speaks of γλαυκώσεες. He and his successors down to Maître Jean, at the beginning of the eighteenth century, confound what was known as glaucoma with cataract, some considering the terms identical, others different.

Brisseau (1709), from the anatomical examination of the eyes of Bourdelot, the blind physician of Louis XIV, showed that the seat of disease was not in the lens. He attributed it to opacity of the vitreous, a view which received the support of Joseph Beer (1792) and was widely accepted on his authority, amongst others by Demours and Middlemore.

An epoch is marked by the observation of the hardness of the globe and the increased watery contents by Mackenzie (1830). He employed puncture of the vitreous for the relief of the condition. Scleral puncture was also used by Middlemore but did not receive general acceptation, and Mackenzie's discovery seems to have fallen into oblivion.

The next period was one in which the cause of glaucoma was attributed to disease of the optic nerve or retina (Wenzel, (1808), Wardrop, (1828), Tyrrell (1840), and others). It was followed by a period in which the choroid was indicted (Lawrence (1833), v. Ammon (1838), Sichel, Arlt).

An epoch was ushered in by the discovery of the ophthalmoscope. The first investigation of glaucoma using this method was by Julius Jacobson (1853). Jaeger (1854) described the glaucoma cup, but fell into the mistake that the appearances were caused by a swelling of the disc. This description was repeated by v. Graefe (1854) in his first paper on the subject, but was quickly corrected in the following year. v. Graefe attributed glaucoma to a serous choroiditis, which caused increase in volume of the vitreous, rise in intra-ocular pressure, and compression of the retina. Mackenzie's discovery was thus resuscitated. v. Graefe (1869) considered that the cause of simple glaucoma was to be found in the sclerotic. Starting from the idea that the deleterious effects of glaucoma were due to the increased tension, he sought for a means of reducing it. Observation of animals in which iridectomy had been performed, and the results of iridectomy in corneal ulceration,

etc., led v. Graefe to the epoch-making discovery of iridectomy as a cure for glaucoma (1856).

Donders (1862) took simple glaucoma as the type of the disease. Here the excavation of the disc was found to occur without any inflammatory symptoms, a result entirely of the increased tension. This was the essential feature of the disease, and it was due to irritation of secretory nerves in the eye. Hence was ushered in the long series of observations upon the conditions of secretion of the intra-ocular fluid, commenced by Wegner (1866), Adamük (1866), v. Hippel and Grünhagen (1866), and continued to the present day (Leber, Parsons, Paterson, Henderson and Starling).

Wegner, from his clinical observations and experimental researches, associated glaucoma with trigeminal neuralgia and increased activity of the secretory nerves. v. Hippel and Grünhagen also attributed the chief *rôle* to the fifth nerve, but admitted that obstruction of the venæ vorticosæ might be a factor.

Meanwhile attention had been drawn to the sclerotic. Cusco (1862), from thickening of the sclera which he observed in glaucomatous eyes, considered that the increased tension was due to retraction of this tissue and diminution in the capacity of the globe. This view was accepted in modified form by Coccius (1863), Adamük (1867), Stellwag von Carion (1868), and v. Graefe (1869).

A variety of other conjectures occur in the literature of the middle of last century. Thus Jaeger (1858) and Hancock (1860) suggested an arthritic dyscrasia, affecting the blood-vessels; the former denied the preponderant influence of the raised tension. Ad. Weber (1868) distinguished a secretory glaucoma due to general angioneurosis, an obstructive glaucoma occurring as a pure ophthalmia, and a congestive glaucoma. Stilling (1868) and Hasner held that glaucoma was a hydrops of the vitreous. de Wecker (1863), Galezowski (1872), and Schweigger (1873) accepted the secretory nerve theory. Schmidt-Rimpler (1877) accepting the generally received view that the essential feature in glaucoma is the increased intra-ocular pressure, found the causes in rigidity and diminished elasticity of the sclerotic, irritation of the fifth nerve, and obstruction to the exit of venous blood from the eye. He held that these factors differ in importance in different cases, and that each case must be judged on its own merits.

A new era had, however, already commenced. In 1876 Max Knies and Adolph Weber, working independently, and following a clue given three years earlier by Leber, discovered the frequency of obstruction of the angle of the anterior chamber in glaucoma. As will be seen in the sequel this obstruction of the filtration angle accounts satisfactorily for nearly all cases of secondary glaucoma. It did not fully account for primary sarcoma, but the researches of Priestley Smith (1879) on the growth of the lens afford a reasonable explanation of the pathogenesis of these cases.

BRISSEAU.—Traité de la Cataracte et du Glaucome, Paris, 1709. BEER.—Die Lehre von den Augenkrankheiten, Wien, 1792. MACKENZIE.—Treatise, 1830. MIDDLEMORE.—Treatise, 1835. WENZEL.—Manuel de l'Oculiste, Paris, 1808. WARDROP.—Morbid Anatomy of the Human Eye, London, 1828. TYRRELL.—A Practical Work on the Diseases of the Eye,

London, 1840. LAWRENCE.—Treatise, 1833. v. AMMON.—Klinische Darstellungen, Berlin, 1838. SICHEL.—Ann. d'Oc., v, vi, vii, viii, x. ARLT.—Prager Vierteljahrsschrift, 1847. JACOBSON.—Dissertation, 1853. JAEGER.—Ueber Staar u. Staaroperationem, Wien, 1854. v. GRAEFE.—A. f. O., i, 1, 1854; i, 2, ii, 1, 1855; iii, 2, 1857; iv, 2, 1858; viii, 2, 1862; xv, 3, 1869. DONDERS.—A. f. O., viii, 2, 1862; ix, 2, 1863; B. d. o. G., 1864. WEGNER, ADAMÜK, AND OTHERS.—See p. 1054. CUSCO.—Ann. d'Oc., xlvii, 1862. COCCIUS.— Ophthalmometrie, Leipzig, 1872. ADAMÜK.—Ann. d'Oc., lviii, 1867. STELLWAG VON CARION.—Lehrbuch, Wien, 1870. JAEGER.—Ueber Glaucom, Wien., 1858. HANCOCK.— Lancet, 1860. AD. WEBER.—B. d. o. G., 1868. STILLING.—A. f. O., xiv, 3, 1868. HASNER. —Prager Vierteljahrsschrift, cvi. DE WECKER.—Traité, Paris, 1863. GALEZOWSKI.—Traité, Paris, 1872. SCHWEIGGER.—Handbuch, Berlin, 1873. SOELBERG WELLS.—Treatise, London, 1870. SCHMIDT-RIMPLER.—In G.-S., v, 1877. KNIES.—A. f. O., xxii, 3, 1876. AD. WEBER. A. f. O., xxiii, 1, 1876. PRIESTLEY SMITH.—Glaucoma, London, 1879, 1891.

"Glaucoma" is the term used in a broad sense for all those conditions in which the intra-ocular pressure is pathologically increased. Used in this wide manner two great classes of cases can be distinguished, viz. (1) those in which the tension is usually only moderately increased, in which the anterior chamber is deep, and in which there are more or less definite signs of inflammation of the ciliary body; and (2) those in which all grades of increased tension are met with, in which the anterior chamber is shallow, and in which, while there may be very evident signs of congestion and irritation, any definite signs of ciliary inflammation are either absent or secondary in onset. It is well to keep these two groups quite separate, since their pathogenesis is different and the differences in clinical history and treatment are marked. The term "glaucoma" proper should be limited to the second group, to which alone it originally applied. It will be well therefore to clear the ground by eliminating the first group, giving briefly the reasons why the raised tension in these cases differs from that in the second group.

It has already been shown that colloid solutions pass much less readily through the filtration angle into the canal of Schlemm than saline solutions or normal aqueous (v. p. 987). Priestley Smith showed that ascitic fluid or blood-serum escaped very slowly from the anterior chamber. It has been shown that in subacute and chronic iridocyclitis—the so-called serous iritis—the aqueous is highly albuminous and contains leucocytes which are often deposited as precipitates—so-called keratitis punctata—upon the posterior surface of the cornea (see Vol. I, p. 349). Under these conditions it is to be expected that the tension of the eye will be raised, and this is found to be the case. Anatomically, the pupil is dilated and the periphery of the iris is displaced backwards, so that the anterior chamber is deep, especially at the periphery, and the filtration angle is widely open, even more widely so than normal. In long-standing cases the optic disc may be cupped exactly as in the typical cases of glaucoma. Here the cause of the increased intra-ocular pressure is undoubtedly the albuminous nature of the lymph which is secreted by the defective ciliary vessels. Whilst the rate of production remains unaltered or even increased owing to greater permeability of the disordered vessels, the outflow at the filtration angle is diminished. This has been held to afford a sufficient explanation of the deepening of the anterior chamber. It is said that the obstruction is at the angle; hence the fluid accumulates in the anterior chamber, and the iris is pressed backwards. I do not consider that

this is an efficient explanation. It will be seen later that the secondary forms of glaucoma are due to mechanical blocking of the filtration angle—*i. c.* by an obstruction which is merely of a different, but still of a physical, nature. It may be said that this blockage precedes the increase in tension, so that the iris can no longer become retracted. It is well known, however, that the adhesion of the iris may be very slight, in some cases a simple apposition, and that it is limited in extent. If the tension becomes increased in such cases, it is difficult to understand why, on the generally received view as to cyclitis, the anterior chamber does not become deep. Further, it is to be remembered that in dealing with the fluid contents of the globe the pressure will be uniformly distributed in all directions. There is no impediment to the passage of fluid through the zonule of Zinn in either group of cases. It seems probable, therefore, that there is some other factor at work besides the abnormal proteid content of the lymph which brings about the deepening of the anterior chamber. In the later stages there is, of course, no difficulty in accounting for the retraction of the iris. The exudates are then becoming organised, and there is a mechanical retraction due to their contraction. This process has not commenced in the early stages, when the chamber is already deep. Indeed, the organisation of the exudates ushers in a phase in which the ciliary body is becoming so disorganised that secretion is diminishing, the tension is reduced to normal, soon becomes permanently subnormal, and the eye shrinks.

A simple, uncomplicated iritis seldom produces so manifest an increase in the intra-ocular pressure. This is due partly to the relatively small amount of exudate poured out into the aqueous, partly to the absorptive capacity of the iris, but mostly to the fact that the ciliary body is little involved, so that the abnormal aqueous is freely diluted with normal lymph secreted at the normal rate.

True glaucoma may be broadly divided into two forms—primary and secondary. Primary glaucoma, acute and chronic, has been called idiopathic, since it comes on without any apparent fundamental cause. Since it is a pathological problem of much greater difficulty and complexity than the secondary form, and since the pathogenesis of the latter throws some light upon that of the former, secondary glaucoma will be considered first.

Secondary Glaucoma.

The chief ætiological precursors of secondary glaucoma are as follows (slightly modified from Priestley Smith) : (1) Annular or total posterior synechia; (2) perforation of the cornea with anterior synechia; (3) dislocation of the lens (*a*) into the anterior chamber, (*b*) laterally : (4) wound of the lens; (5) operations upon the eye; (6) intra-ocular tumours; (7) intra-ocular hæmorrhage; [(8) detachment of the retina]; (9) aniridia.

Seeking now for the proximate causes of increased intra-ocular pressure, since the normal pressure is maintained by a production of lymph which is accurately balanced by an equivalent excretion, subject

only to slight and transitory modifications which are rapidly and efficiently compensated, it is clear that a pathological increase of pressure must be due to (A) increased production associated with normal or diminished outflow, to (B) diminished outflow associated with normal or increased inflow, or to (C) increased production associated with diminished outflow. Summarising the results arrived at in the previous chapter, (A) may be due to (1) increased general blood-pressure; (2) local dilatation of the arterioles of the ciliary body; (3) increased permeability of the local capillary walls; (4) constriction or obstruction of the local efferent veins. (B) may be due to obstruction of the filtration angle, either (1) mechanical—(a) blockage of the spaces of Fontana with leucocytes, red corpuscles, pigment, etc.; (b) peripheral
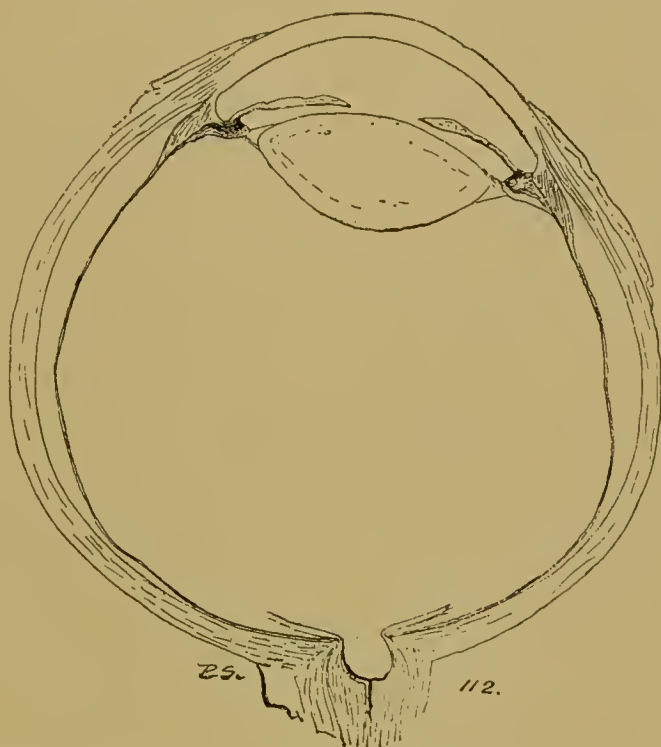
FIG. 721.—IRIDO-CYCLITIS.
From Priestley Smith. From an eye with increased tension and cupped disc due to irido-cyclitis. The filtration angle is widely open.

anterior synechia; or (2) physical—an albuminous aqueous; and (C) may be due to the combination of any of the factors causing (A) with any of the factors causing (B).

It has already been pointed out that the factors (A) (3) and (B) (2) actually come into play in subacute and chronic iridocyclitis, and that they produce a clinical picture which differs in many essentials from that of true glaucoma. Whilst admitting that it is highly probable that these factors play some part in many cases of true glaucoma, they must be eliminated as *causa causans*.

Considering the importance of the general blood-pressure and local vascular conditions in the maintenance of the intra-ocular pressure, it is not surprising that the early observers sought the *causa causans* of

glaucoma here. Such ideas, indeed, prompted the researches of Wegner, Adamük, v. Hippel and Grünhagen, and others. As regards the general blood-pressure, the extraordinarily sensitive mechanism for compensation of sudden or large changes in pressure afforded by the control of the vasomotor centre renders it improbable, or even impossible, that continued high intra-ocular tension can be due to this cause alone. It is essential that there should be some local mechanism also at work. It has been shown that there is no evidence of secretory nerves, nor even any incontrovertible evidence of specific vaso-dilator nerves. It is
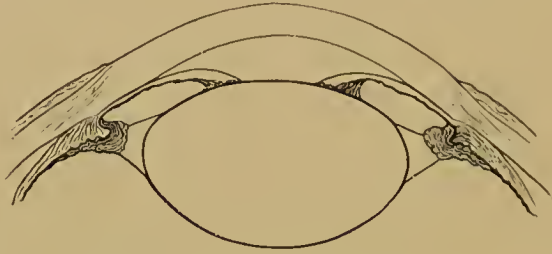
FIG. 722.—SECLUSIO PUPILLÆ.
From Lawson, after Priestley Smith.

true that there are vaso-constrictor nerves, and it is probable that they have a tonic action; section or disease of these nerves might bring about loss of tone in the ciliary vessels, which would manifest itself by slightly increased pressure, but such a mechanism would fail wholly to account for the continued high tension of glaucoma. It will be shown that the one common feature in the morbid anatomy of secondary glaucoma is the apposition or adhesion of the periphery of the iris to the cornea, first described by Knies and Weber. That this blockage of the filtration angle is amply sufficient to account for the prolonged
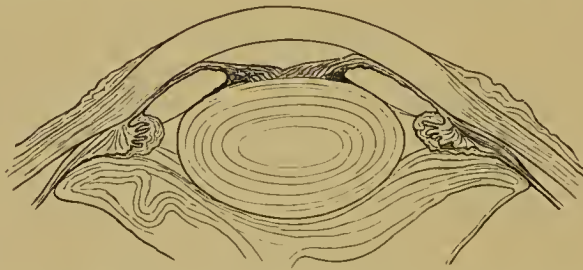
FIG. 723.—SECLUSIO AND OCCLUSIO PUPILLÆ.
From Lawson, after Priestley Smith.

raised tension is shown by many observations. Thus, Priestley Smith showed that if the eye is injected through two cannulæ, one in the anterior chamber and one in the vitreous, then a very slight excess of pressure in the vitreous forces the periphery of the iris against the cornea and almost or quite abolishes filtration. Moreover, Bentzen and Leber showed that filtration from the anterior chamber was much diminished in enucleated eyes having this peripheral annular anterior synechia. Further, Wagenmann and Leber occasionally obtained such an adhesion accidentally in rabbits, and found that it was followed by all the symptoms of glaucoma, including cupping of the disc. Finally,

Heisrath and Bentzen succeeded in producing peripheral annular anterior synechia in rabbits experimentally without arousing much inflammatory reaction; it was followed by permanent increase of tension and marked diminution of filtration.

On the other hand, it has been pointed out that peripheral anterior synechia may be met with in eyes which have no history and present no signs of glaucoma. The explanation in most of these cases is that the adhesion is not annular; part of the circumference is open, so that sufficient fluid escapes to prevent a pathological rise of pressure.
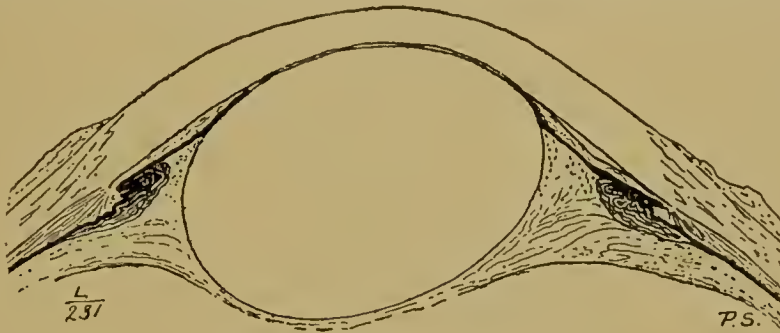
FIG. 724.—SECONDARY GLAUCOMA.

From Priestley Smith. Wound of the cornea; permanent abolition of the anterior chamber; access of fluid to the filtration angle completely cut off.

In other cases the ciliary body is diseased and disorganised or degenerated, so that the rate of production of lymph is sufficiently diminished. In yet other cases it is probable that some abnormal modes of absorption or channels of escape have developed. Often the cornea is transformed into a mass of highly vascular fibrous tissue, no longer lined by impermeable endothelium; these new vessels probably absorb much of the fluid. In other cases there is some form of filtering scar.

It will be well now to consider *seriatim* the chief causes of secondary
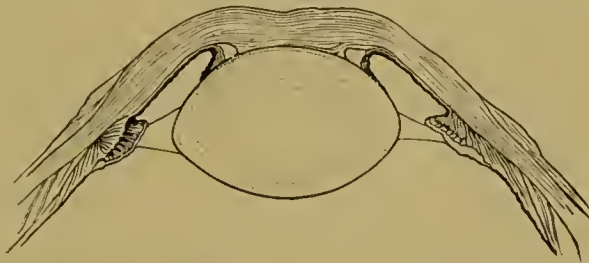
FIG. 725.—PERFORATION OF THE CORNEA.

From Lawson, after Priestley Smith. The iris is adherent to the cornea, and there is a ring posterior synechia; the lens is adherent to the pseudo-cornea.

glaucoma, and to explain the rationale of the production of increased intra-ocular pressure in the individual forms.

Annular posterior synechia (*see* Vol. I, p. 289, Figs. 187, 188).—In this condition there is seclusion or shutting off of the pupil. The lymph secreted by the ciliary body is unable to pass through the pupil and is dammed back behind the impermeable iris, which becomes bulged forward like a sail (iris bombé). The tension rises, and if the condition is not speedily relieved the periphery of the iris becomes apposed to the

cornea and may later become adherent to it. If a satisfactory artificial opening is made in the iris in the early stage, the iris retreats, the angle is reopened, and the tension becomes again normal. If the tension has persisted for a considerable period, the operation may leave the pressure subnormal, showing that the ciliary body has been injured and its secretory function impaired. If it has persisted still longer, all the sequelæ
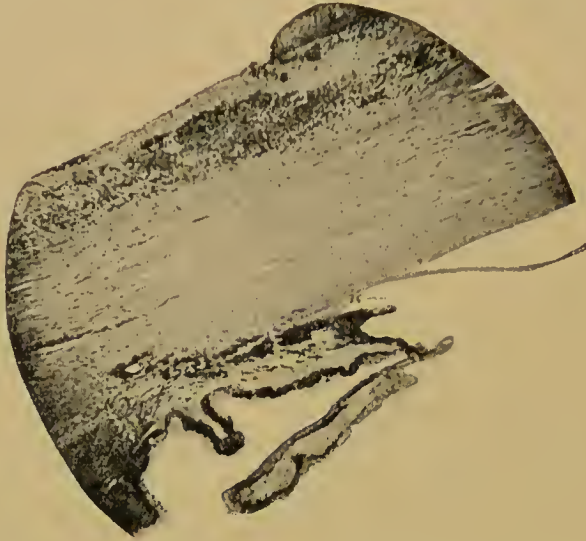
FIG. 726.—GLAUCOMA OF THE CORNEAL WOUND.

Treacher Collins, Researches. The whole iris escaped through a wound in the cornea. The filtration angle is blocked by ciliary processes, which are displaced forwards.

of glaucoma, with cupping of the disc, etc., ensue, and relief can only be obtained, if at all, by a wide and peripheral iridectomy which will again open up the occluded angle. Since the adhesion of the iris to the cornea is now much firmer, the prognosis of operative interference is so much the worse.
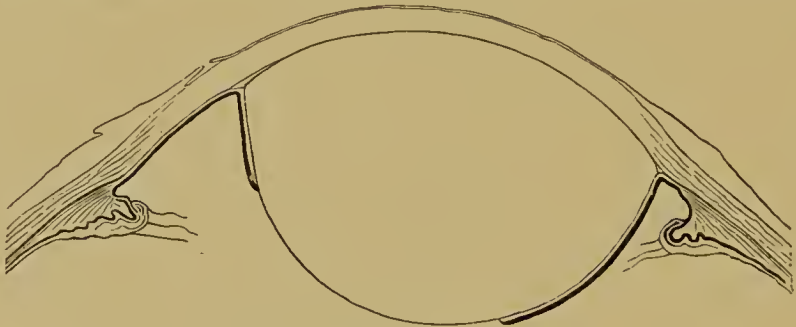
FIG. 727.—SECONDARY GLAUCOMA.

From Priestley Smith. Spontaneous dislocation of the lens into the anterior chamber in a patient æt. 55, with retinitis pigmentosa.

Perforation of the cornea with anterior synechia.—Perforation of the cornea as the result of wounds or ulcers may cause secondary glaucoma in a variety of ways. In all the essential factor will be found to be a widespread obstruction to the filtration angle. Thus prolapse of iris causes temporary, and it may be permanent, obliteration of a

large area. Even if the area is small at first it is liable to spread owing to the iritis which is set up (*see* "Complicated Wounds of the Cornea," vol. i, p. 156). The lens may be carried forward so that the anterior chamber is abolished, and this condition may persist, especially if, as is frequently the case, the lens is also wounded. Central ulcer of the cornea may lead to adhesion of the lens and iris (*see* Vol. I, Fig. 94).

FIG. 728.—SECONDARY GLAUCOMA.
From Priestley Smith. Lateral dislocation of the lens by a blow.

In anterior staphyloma (q.v., Vol. I, p. 168) the anterior chamber is partially or completely obliterated. The condition usually arises early in life, when the walls of the globe are more plastic than at a later date ; moreover the ciliary body is generally seriously affected. Hence, on the one hand the rise of tension which occurs leads to stretching of the globe, especially of the pseudocornea, so that the usual anatomical features of glaucoma may be modified, though the disc is almost invari-
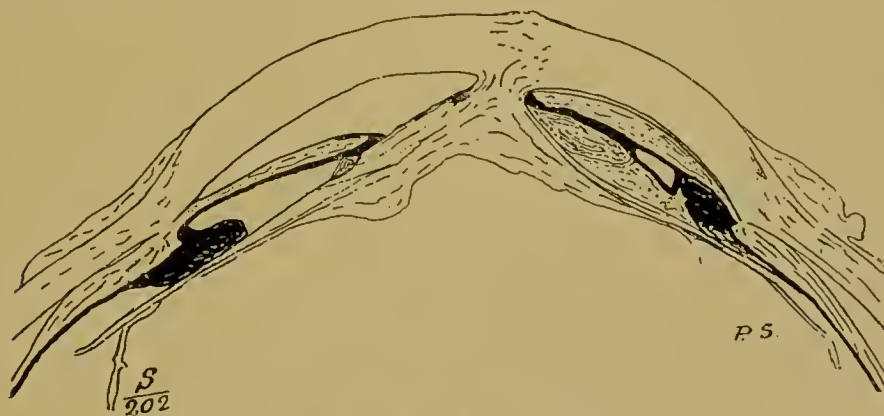
FIG. 729.—SECONDARY GLAUCOMA.
From Priestley Smith. Puncture of cornea and lens with scissors ; adhesion of capsule and vitreous to cicatrix.

ably cupped; on the other hand, the production of lymph may be diminished so that the tension is not pathologically increased.

Dislocation of the lens into the anterior chamber.—Dislocation of the lens may be spontaneous, when the lens is shrunken from any cause, or it may be traumatic. If the lens is very small, it may set up little or no reaction, and glaucoma does not occur. If the irritation of

the iris is considerable, the iritis, combined with the presence of the lens, may cause occlusion of the angle. If the lens is of considerable size, the obstruction to filtration will be so great that glaucoma rapidly supervenes. The lens becomes moulded to the cornea, and the iris is firmly applied to its posterior surface, the contraction of the sphincter iridis, indeed, forcing the lens closely into apposition to the cornea. A case has been recorded in which no glaucoma occurred until eserin was
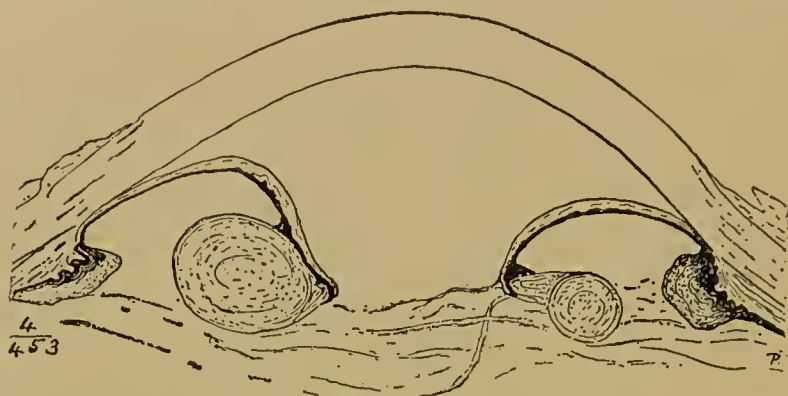
FIG. 730.—SECONDARY GLAUCOMA.
From Priestley Smith. Discission for cataract in infancy—seven years before excision. Annular posterior synechia; bombé iris.

instilled (Minor). On the other hand, the tension is sometimes relieved by atropin.

Lateral subluxation of the lens.—Here the normal lens is forced to one side by a sudden blow upon the eye. If the lens is well supported behind by a consistent vitreous, it will press upon a considerable area of the circumference of the ciliary body and iris, so that a large part of the filtration angle will be blocked. This is found to have occurred in those cases where glaucoma has supervened which have been examined
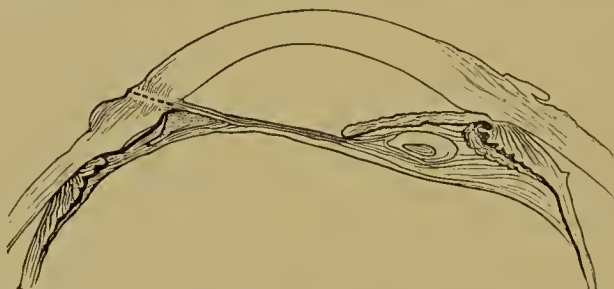
FIG. 731.—GLAUCOMA AFTER EXTRACTION.
From Lawson, after Priestley Smith. Capsular synechia.

anatomically. Glaucoma has been known to occur in a case of a congenitally displaced lens (Bowman).

BOWMAN.—R. L. O. H. Rep., v, 1865.

Wound of the lens.—When the lens is wounded by accident or by mischance during operation it swells up and presses the iris against the cornea (see "Traumatic Cataract," vol. ii, p. 417). Under these circumstances glaucoma will almost inevitably follow. Even when the

wound is small and limited to the anterior capsule and pupillary area glaucoma may occur, as is often seen after rather free discission. Here the iris may not necessarily be pressed against the cornea, but the filtration angle is blocked by masses of swollen lens-fibres, which filter through extremely slowly. That this accounts for the rise of tension

FIG. 732.—GLAUCOMA AFTER EXTRACTION.
From Priestley Smith. Iris and vitreous adherent to cicatrix.

is shown by its prompt relief when the lens matter is let out by a curette evacuation.

Post-operative glaucoma.—Intra-ocular operations are occasionally followed by glaucoma independently of blockage of the angle, owing to swelling of the lens.

(A) *After extraction of cataract.*—Bowman (1865) mentioned that glaucoma was particularly apt to come on after needle operations

FIG. 733.—GLAUCOMA AFTER EXTRACTION.
From Priestley Smith. Exudates and lens matter in a.c.

following flap extraction, and he points out that it is by no means an indication or mere result of iritis; v. Graefe (1869) also found that it was not rare after extraction or discission; he attributed it to swelling of remnants of cortex and to displacement of the capsule, with traction and irritation of adherent ciliary processes. Priestley Smith recorded a case in 1879 after extraction of senile cataract; he considered that plastic iritis bound down the iris to a thickened capsule. An impervious

partition is thus formed, behind which fluid accumulates, as in bombé iris, and the angle is blocked by the same mechanism. Since that time he has recorded other cases (1891). Stölting (1887) found incarceration of iris and capsule in the cicatrix in one case examined ; he considered that it was due to traumatic choroiditis, the occlusion of the angle being secondary. Treacher Collins (1888, 1890, 1905) has examined a considerable number of cases. In the cases of senile cataract extracted at Moorfields from 1885 to 1889, 1405 in number, 9, or 0·64 per cent., were lost from glaucoma. Natanson (1889) collated and analysed the records of thirty-seven cases. These show that immunity from subsequent glaucomatous complication is not insured by any particular method of operation ; it may occur after extraction, with or without iridectomy, after extraction preceded by a preliminary iridectomy, or after extraction in the capsule. In the majority there was some visible complication involving the iris or capsule, or both. In some cases no visible adhesion
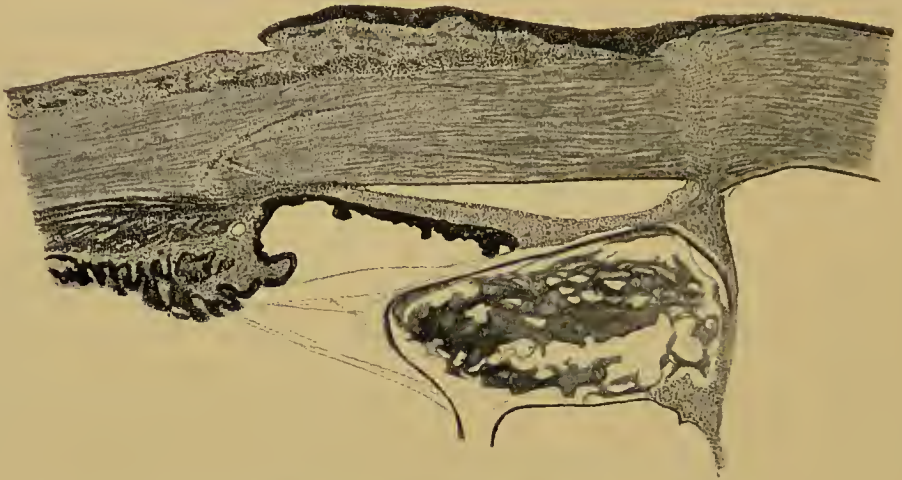
FIG. 734.—GLAUCOMA AFTER EXTRACTION.
Treacher Collins, Researches.   Adhesion of the lens capsule to the scar.

of iris or capsule could be found. It has been shown, however, by Becker that capsular synechia may be undiscoverable in the living eye.

From a review of the cases reported, it would seem that the common feature present in all is incarceration of capsule or iris, or both. This condition, if limited in extent, may lead to no evil results. It may, on the other hand, cause increased tension in two ways—(1) by setting up a severe iridocyclitis ; (2) by causing sufficient blocking of the angle to bring about secondary glaucoma.

In all the cases reported by Treacher Collins there was some adhesion of the capsule or iris to the cicatrix. Usually the angle was blocked in the whole area of the coloboma. In some the angle was occluded over a much wider extent. In such cases secondary glaucoma must inevitably supervene. In others the remainder of the angle was open, and probably a sufficient area was patent to permit free filtration. In these increased tension is the result of iridocyclitis. It has already been pointed out that incarceration of capsule, etc., in a wound much retards and impairs satisfactory cicatrisation (v. Vol. I,

p. 156, *sqq.*). The scar remains weak and spongy ; on the one hand, it is liable to become ectatic under normal intra-ocular pressure ; on the other, if by any means the superficial epithelium is injured, an easy route is opened up for the penetration of pathogenic organisms. Further, the anchoring of the suspensory ligament to the cicatrix causes a continual drag upon the ciliary processes, exaggerated by the perpetual movements of the iris and ciliary muscle. In this manner ciliary irritation is set up, which the entry of pathogenic organisms may transform into a severe iridocyclitis.

Treacher Collins has shown that either or both ends of the divided anterior capsule may become agglutinated to the posterior surface of

FIG. 735.—GLAUCOMA AFTER EXTRACTION.
Treacher Collins, R. L. O. H. Rep., xvi ; from a photograph by Collier Green. The external part of the wound has united ; some downgrowth of superficial epithelium is seen. The posterior part of the wound gapes widely, and the peripheral part of the anterior capsule is lying in it, surrounded by much cellular exudation.

the wound, or the inflammatory exudate on the posterior surface of the wound may extend between the two lips of the divided anterior capsule and unite the posterior capsule to it. The agglutination of the capsule to the wound does not delay its healing as entanglement in the wound does. On the other hand, it considerably advances the position of the lens capsule, and with it the position of the iris. In some cases this is sufficient to bring the root of the iris into apposition to the posterior surface of the cornea. Even where the iris is absent in the coloboma either a small stump of iris or the ciliary processes are dragged forwards. The more the advance of the capsule, and secondarily of the iris, the greater is the probability of the onset of glaucoma. Hence corneal sections are more dangerous than those in the corneo-scleral margin.

Sometimes in eyes with adherent capsule the tension does not rise until after needling. In some of these cases Collins found a fresh adhesion of capsule to the discission wound; this is an additional argument in favour of entering the needle at the limbus in these cases.

Adhesion of capsule may occur when no iridectomy has been performed; in one such case the vitreous was adherent to the scar. Agglutination of the capsule to the wound is most likely to occur when re-formation of the anterior chamber has been delayed.

Another cause of glaucoma after extraction of cataract and other operations in which the anterior chamber is opened is the downgrowth of epithelium into the anterior chamber, which it may finally line com-

Fig. 736.—IRIDOCYCLITIS AFTER EXTRACTION.
Treacher Collins, R. L. O. H. Rep., xvi ; from a photograph by Collier Green.
The external part of the wound has united. The lips of the posterior part are much
swollen and infiltrated, and gape widely ; the peripheral part of the anterior capsule
passes forwards between them.

pletely (v. Vol. I, pp. 163, 253, 312). Fluids are unable to filter through the epithelium and glaucoma is thus induced.

(B) *After iridectomy.*—Glaucoma may recur after iridectomy which has been performed for the relief of that condition, and may be the result of complications of the actual operation. Apart from accidental wounding of the lens, this may be due to various causes, all, however, leading to closure of the filtration angle. Thus, the iris may not have been removed up to its extreme periphery, so that a portion is left blocking up the filtration area, often rendered additionally secure in its faulty position by entanglement of the cut edge in the scar. Sometimes the anterior chamber is very slow in re-forming ; the lens may then become anchored to the wound by exudates, which subsequently

organise and pull the lens, and with it the root of the iris and ciliary processes, still farther forwards. If the section has been very peripheral, prolapse or adhesion of the ciliary processes may occur, even if the iris has been removed quite up to the periphery.
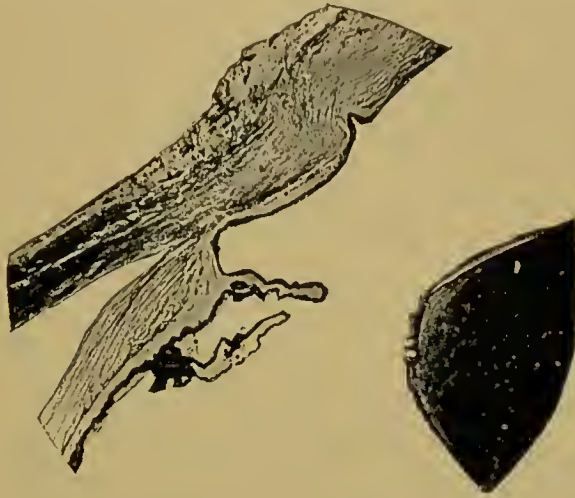
FIG. 737.—GLAUCOMA AFTER IRIDECTOMY.

Treacher Collins, Researches. Subacute glaucoma; return of tension after operation; excision two months later. A large portion of the periphery of the iris has been left, and is blocking the filtration angle, the cut end being adherent to the cicatrix.

FIG. 738.—GLAUCOMA AFTER IRIDECTOMY.

Treacher Collins, Researches. Absolute glaucoma; return of tension after operation; excision one year later. Lens capsule adherent to cicatrix; filtration angle blocked by ciliary processes.
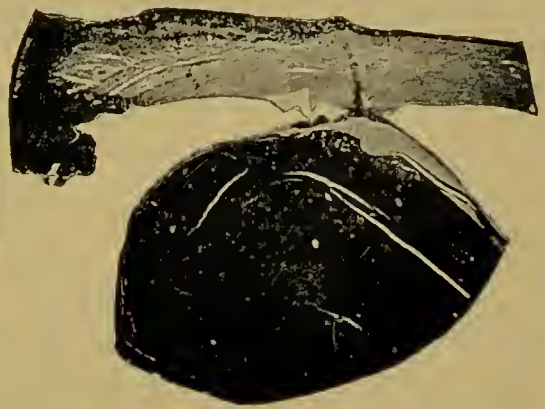
FIG. 739.—GLAUCOMA AFTER IRIDEC-
TOMY.

Treacher Collins, R. L. O. H. Rep., xiii. Showing adhesion of lens capsule to iridectomy cicatrix.

The danger of glaucoma following iridectomy for purposes other than the relief of glaucoma is much less. The eyes are usually in a more healthy condition and the wound is less peripheral. When it does occur the same factors will be found at work.

Intra-ocular tumours.—In discussing intra-ocular tumours it has already been pointed out that if the eye is retained sufficiently long glaucoma supervenes (*see* "Tumours of the Iris, Ciliary Body, Choroid, and Retina"). In tumours of the iris there is blocking of the angle and often infiltration of the canal of Schlemm and neighbouring parts. In tumours of the choroid the angle is usually blocked by the advance of the iris following detachment of the retina and pressure upon the vitreous. Glaucoma may come on early in some of these cases—*i. e.* at a
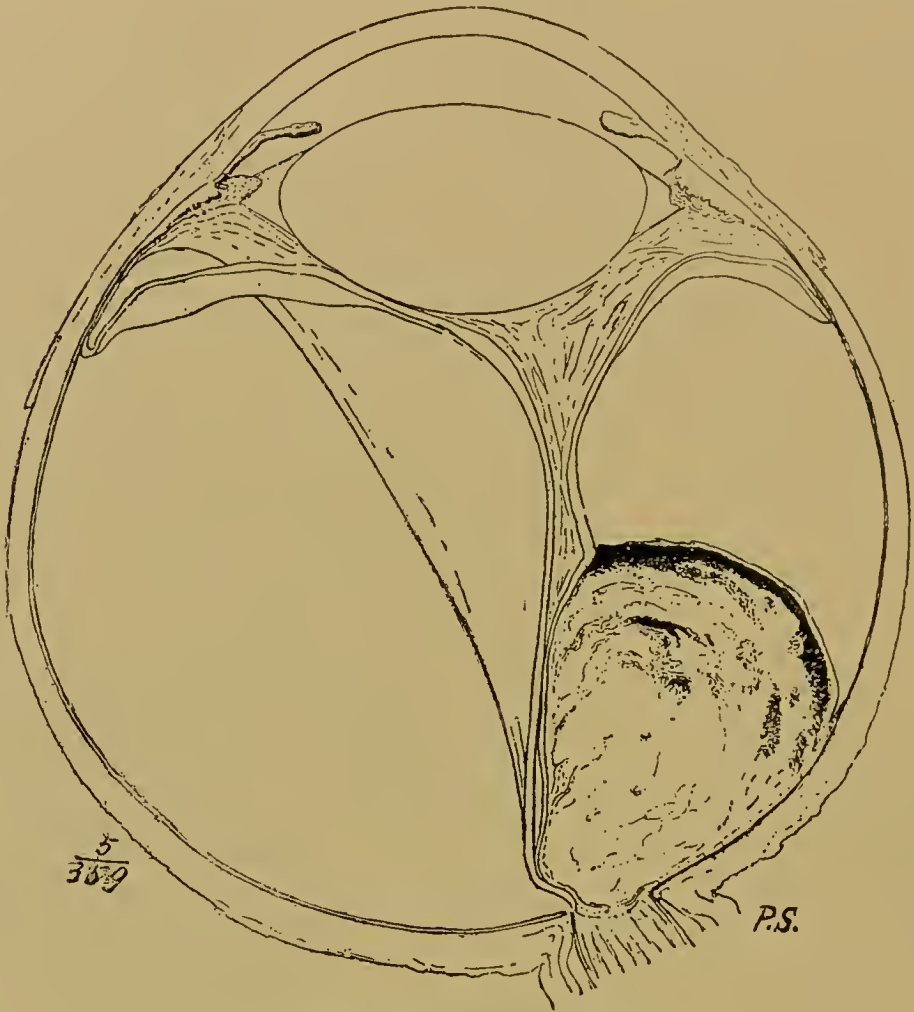
FIG. 740.—SECONDARY GLAUCOMA.
From Priestley Smith. Following sarcoma of the choroid.

period when the detachment is comparatively small. These cases are sometimes to be explained by the proximity of the tumour to a vortex vein, which is thus obstructed so that the intra-ocular tension rises. Additional factors in the genesis of glaucoma in the presence of sarcoma of the choroid are found in the deposits of leucocytes, pigment, etc., in the angle, iritis, etc. (*see* Vol. II, pp. 498, 523, 529). Glaucoma is somewhat delayed in tumours of the ciliary body by the late onset of retinal detachment. The tumour may, however, invade the anterior chamber, causing obstruction of the angle in the same manner as in the case of

tumours of the iris. In glaucoma resulting from glioma of the retina the same mechanism is at work as in sarcoma of the choroid. There is the same invasion of the vitreous chamber, an invasion which is at first readily compensated by expression of the fluid contents. When only the resistant vitreous tissue remains the lens and iris are forced forwards and the angle becomes blocked. Additional factors are found in the greater concentration of the aqueous, the presence of glioma-cells in the angle, involvement of the iris, etc. (*v.* Vol. I, p. 332).

It must be conceded that the onset of glaucoma in many cases of intra-ocular tumours is not altogether satisfactorily explained. The reasons already given suffice to account for the majority of cases, but detailed examination of the actual processes at work shows that the

FIG. 741.—GLAUCOMA WITH ANIRIDIA.
Treacher Collins, Researches. The angle of the anterior chamber is seen to be blocked by a rudimentary iris. The ciliary body has become detached from the sclerotic during the preparation of the specimen.

mechanism is not always so simple (*v.* Vol. II, p. 523). The subject would repay further investigation.

Intra=ocular hæmorrhage.—It is easy to understand why intra-ocular hæmorrhage causes glaucoma. If the hæmorrhage is considerable, the intra-ocular tension is suddenly raised to a point not far removed from the pressure in the arterioles. It is not uncommon in old blind eyes for the degenerated vessels to give way on slight provocation, such as a relatively feeble blow upon the eye. Here the eye becomes hard and extremely painful. In these cases the bleeding is undoubtedly arterial. The hæmorrhage may be from retinal vessels into the vitreous, but this is probably more frequently venous, and does not necessarily give rise to glaucoma. In most cases it is subchoroidal, the choroid and retina being detached and the vitreous forced forwards, so that not only is the

eye subjected to the direct blood-pressure, but the angle is obliterated and all exit of fluid is abolished.

Detachment of the retina.—It might be thought that detachment of the retina would cause glaucoma in the same manner that this condition is induced in the presence of intra-ocular tumours, for in the latter case the increase in tension is intimately associated with the detachment. This is by no means the case. It is very rare for a simple detachment to cause glaucoma; on the contrary, the tension is usually subnormal. Thus, in 126 cases collected from Leber's clinic at Göttingen, very carefully investigated by Nordenson, increased tension was present in only 6. Of these, 1 had irido-cyclitis, with occlusion of the pupil and bombé iris, in 3 there was acute iridocyclitis, with deep anterior chamber, in 2 the cause was not satisfactorily explained. The subject of detachment of the retina is an extremely difficult one, and the question of tension in these cases is complex. The whole subject will be discussed in detail elsewhere.

Aniridia.—Glaucoma may occur both in cases of traumatic and congenital aniridia; indeed, in the latter group there seems to be a marked predisposition. *A priori* it is difficult to imagine how the angle can be blocked in these cases, but the difficulty disappears when microscopical examination is made.

FIG. 742.—GLAUCOMA WITH COLOBOMA OF THE IRIS.

Treacher Collins, T. O. S., xiii. From an eye with coloboma of the iris and lens, in which glaucoma supervened. The iris is absent, but the filtration angle is blocked by a fold in which the ciliary body terminates. The ciliary processes slant backwards.

Treacher Collins has reported two cases of *traumatic aniridia* in which glaucoma supervened. In both the lens had been wounded, and a broad adhesion of the capsule to the scar resulted. In the escape of the iris from the wound, which was near the centre of the cornea, the anterior part of the ciliary body had been drawn forwards, the advance in position being maintained by the capsular synechia. In both specimens the most anterior of the ciliary processes were in contact with the ligamentum pectinatum.

It has already been stated that congenital aniridia has been examined histologically by various observers. In all cases some rudiment of iris was present, and in all the development of the ligamentum pectinatum was faulty. The stump of iris is often adherent to the sclera at the extreme limit of the anterior chamber for a considerable part of the circumference, part of the angle is usually open, and through this efficient filtration is maintained until some intercurrent cause leads to obliteration. There is at present not sufficient evidence to decide between intrauterine inflammation and delayed separation of the iris as the cause of the adhesion. The fact that it exists suffices to explain the tendency to glaucoma; probably a very slight iritis or cyclitis would effect complete closure throughout the circle, either by completing the adhesion or by blocking the filtration meshwork with leucocytes, pigment, or other products of inflammation.

There are other causes of secondary glaucoma, as, for example, that following thrombosis of the central vein of the retina. These will be more conveniently discussed in immediate relationship with the causes.

PRIESTLEY SMITH.—Glaucoma, London, 1891. BENTZEN AND LEBER.—A. f. O., xli, 3, 1895. WAGENMANN.—A. f. O., xxxiv, 1, 1888. LEBER.—Die Entstehung der Entzündung, Leipzig, 1891; in Berberich, A. f. O., xl, 2, 1894. HEISRATH.—C. f. d. med. Wissenschaft, 1879. BENTZEN.—A. f. O., xli, 4, 1895. MINOR.—New York Med. Jl., 1881. BOWMAN.— R. L. O. H. Rep., iv, 1865. v. GRAEFE.—C. f. d. med. Wiss., 1869; R. L. O. H. Rep., viii, 1875. STÖLTING.—A. f. O., xxxiii, 1, 1887. TREACHER COLLINS.—R. L. O. H. Rep., xii, 1888; T. O. S., x, 1890; Researches, London, 1896; R. L. O. H. Rep., xvi, 1905. NATANSON.—Ueber Glaucom in aphakischen Augen, Dorpat, 1889. NORDENSON.—Die Netzhautablösung, Wiesbaden, 1887.
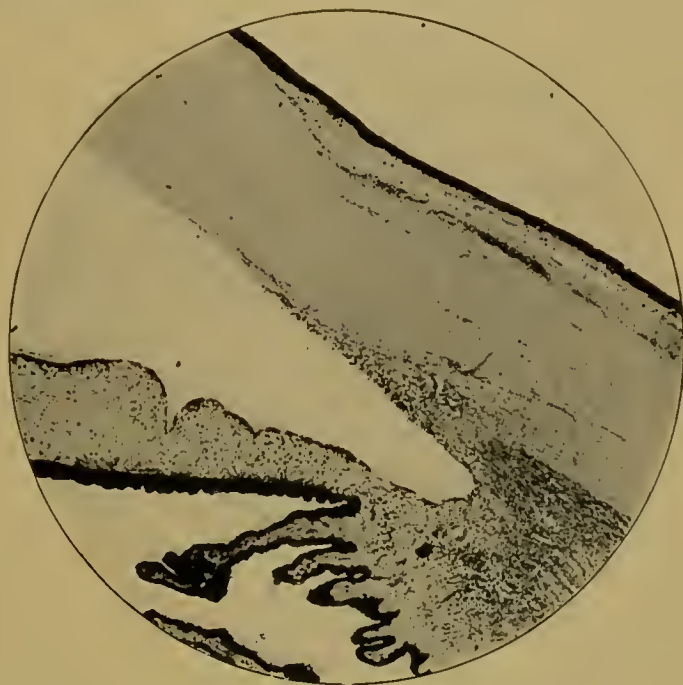
FIG. 743 —NORMAL ANGLE OF ANTERIOR CHAMBER. × 34.
From a specimen by Lister. The eye was normal apart from extensive pigmentation of the conjunctiva and epithelium of the cornea. There are a few scattered pigment-cells upon the ligamentum pectinatum iridis. Schlemm's canal is normal.

PRIMARY GLAUCOMA.

Primary glaucoma is that form of glaucoma in which no antecedent disease can be discovered in the patient to account for the onset of the disorder. Since the problem of the causation of this form is one of great difficulty, it will be well first to review the pathological anatomy.

Pathological anatomy.—It has already been explained that the haziness of the cornea which is met with in the early stages of glaucoma, and which can be reproduced in any excised eye by pressure upon the globe, but which disappears at once when the pressure is removed, is due to increased double refraction of the lamellæ (v. p. 999). The loss of sensitiveness in the cornea during attacks is due to the compression and maceration of the nerve-filaments by fluid which collects in the

nerve-canals in Bowman's membrane, and to their rupture when the epithelium is raised (Fuchs). It is possible that the function of the nerves may also be abrogated by pressure against the sclerotic (Treacher Collins); this would also account for the paralysis of the iris and ciliary muscle, paralysis of accommodation being often an early symptom. The iridescent vision is due, according to Treacher Collins, to the slight disturbance of the epithelium, which is the first stage of corneal œdema. By applying to the normal eye a single drop of a 0·125 per cent. solution

FIG. 744.—PRIMARY GLAUCOMA.
From Priestley Smith. Acute glaucoma; excision ten days later. Ciliary processes swollen and advanced; iris apposed to, but not adherent to, cornea.

of erythrophlœin hydrochlorate slight anæsthesia and haze of the cornea are produced, and well-marked coloured rings are seen round a flame. The same result occurs whether the pupil is constricted or dilated and also in the absence of the lens. In all cases the red ring is outermost, as in glaucoma. The more permanent clouding which results from prolonged high tension is at first due to œdema (v. Vol. I, p. 175); this is followed by vesicular and bullous keratitis, and finally by vascularisation and pannus degenerativus (v. Vol. I, p. 196).

The fact that in secondary glaucoma the angle of the anterior

FIG. 745.—PRIMARY GLAUCOMA.
From Lawson, after Priestley Smith. Chronic glaucoma of twelve months' duration; blind five months; painful three weeks. Base of iris adherent to cornea; ciliary processes atrophied.

chamber is almost invariably found closed has led to much attention being directed to its condition in the primary form. As already stated, the discovery of the importance of this factor was independently brought forward by Knies and Ad. Weber in 1876. Since that time many communications have been made upon the subject, notably in the earlier days by Priestley Smith, Brailey, and Birnbacher and Czermak. Unfortunately, the eyes are always examined at a late stage of the disease. Priestley Smith records the condition of the filtration angle
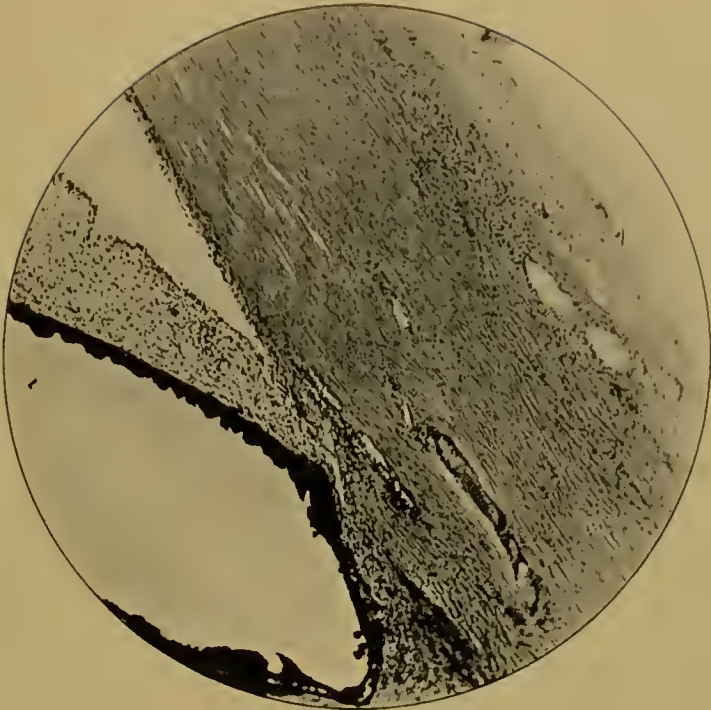
FIG. 746.—PERIPHERAL ANTERIOR SYNECHIA.   × 55.

Secondary glaucoma from detached retina following a blow.   27, i, 1900, blow ;
11, ix, 1900, detached retina seen ; 24, iii, 1902, inflammation.   T + 2.   Narrow
peripheral anterior synechia ; the adherent iris is more degenerated than in Fig. 204.
Schlemm's canal is open, but surrounded by infiltration.
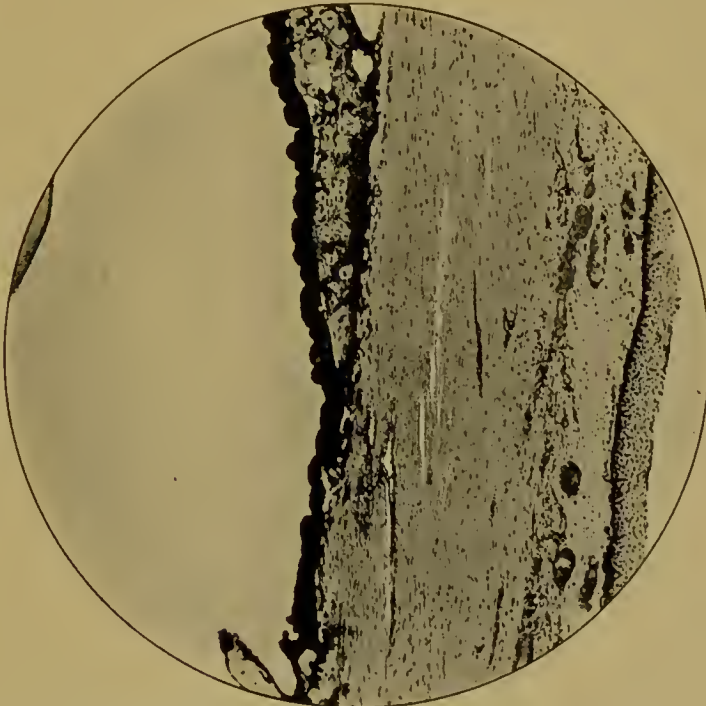
FIG. 747.—PERIPHERAL ANTERIOR SYNECHIA.   × 55.

Old glaucoma ; extensive peripheral anterior synechia, with almost complete
atrophy of part of adherent iris.   The iris elsewhere is degenerated ; note hyaline
degeneration of walls of vessels.   Schlemm's canal infiltrated.

in thirty-four specimens ; the eyes were hardened in Müller's fluid and divided when frozen. In the majority of cases the angle was closed, and when not closed it showed signs of compression. If the glaucoma has been of short duration, the base of the iris may be merely pressed against the margin of the cornea and ligamentum pectinatum, and may

FIG. 748.—NORMAL CILIARY PROCESSES.
Priestley Smith, R. L. O. H. Rep., x.

easily separate in the bisected eye. In older cases it is usually adherent and often much atrophied. The extent of the adhesion varies much in different eyes and in different parts of the same eye. In some cases it involves the periphery of the iris to a width of 1 mm. or more ; in others it is so slight as to be readily overlooked. Sometimes the base

FIG. 749.—CILIARY PROCESSES IN PRIMARY GLAUCOMA.
Priestley Smith, R. L. O. H. Rep., x.

of the iris adheres to the ciliary processes and is drawn backwards when they retract, so that its adhesion to the cornea is more or less torn through ; or if not torn through the iris base may be stretched in the direction of its thickness and present a peculiar bend or notch in its anterior surface at the limit of the adhesion. The adhesion forms most

constantly and most rapidly in acute and subacute cases, as might naturally be expected from the greater congestion and exudation. In the chronic non-irritative form it occurs later, and sometimes not at all, but even in these cases signs of compression of the filtration angle are usually visible (Priestley Smith). (*See* Vol. I, p. 304.)

The iris shows signs either of acute congestion or advanced degeneration, with ectropion of the uvea, etc. (*See* Vol. I, p. 300.)

The ciliary processes are usually altered both in size and position. If the glaucoma has been recent and of the congestive type, they are enlarged and their apices extend forwards far beyond the normal limit. In such cases they are usually in close contact with the iris anteriorly, and sometimes with the margin of the lens internally ; or if not in actual contact their wedge-like shape shows that in the living eye they have been tightly pressed between these structures (Priestley Smith). In transverse section they are seen to be increased in thickness, the spaces between them being narrowed, or even obliterated, by the swelling of the lateral convolutions. If the glaucoma has been of long standing, the processes are sometimes much shrunken and retracted, but even in such cases the iris often bears the impress of their former contact. In the more advanced cases of this type the tension is usually little raised, the secretory functions of the ciliary body being more or less impaired. The ciliary muscle is at first drawn forwards, but later retracts and atrophies (Brailey).

The lens is sometimes found in close contact with the ciliary processes and iris ; more often it is somewhat separated from them, receding when the glaucomatous pressure is removed. In some cases there is an obvious disproportion between the size of the lens and the size of the eye (Priestley Smith, *v. infra*).

The whole of the uveal tract shows changes which may be divided into congestive and degenerative, the former preponderating in the acute congestive forms, the latter in the later stages of these forms and in chronic glaucoma. In the former there is marked venous stasis, often with hæmorrhages. The tissues are swollen by œdematous exudates containing fibrin, leucocytes, red corpuscles, etc. The degenerative changes which have been described in the iris and ciliary body are also manifest in the choroid, which becomes much thinner than normal. Birnbacher and Czermak described changes to which they attached great importance in the vortex veins. Their perivascular lymph-spaces and the surrounding sclerotic were densely infiltrated with round cells, and round and oval cells pervaded the vessel-walls. Great proliferation of the endothelium within the veins was noted in the more advanced cases. These changes were held to originate a venous stasis. That they often occur in old age is undoubted, but they are frequently found in eyes which are quite free from glaucoma (*cf.* Stirling).

In advanced cases of glaucoma the retina is atrophic. Berenstein described in chronic congestive and E. v. Hippel in acute glaucoma a marked obliquity of the outer limbs of the rods and cones. In Berenstein's case—with iridocyclitis—the changes were found over the whole retina ; at the equator the rods and cones were matted together and lay

almost parallel to the surface. In acute glaucoma E. v. Hippel found the rods and cones directed away from the fovea in its immediate vicinity —*i. e.* towards the nasal side nasally, and towards the temporal side temporally. The changes are attributed to the effects of raised intra-ocular pressure. The eyes were placed direct into formol. The sub-ject requires further investigation, particularly taking into account the loss of tissue tension following removal of the eye (*v.* p. 1043, Nicolai, Koster Gzn).

The effect of glaucoma upon the optic nerve was early recognised (H. Müller, 1856). The optic nerve entrance is the weakest spot in the fundus, so that increased intra-ocular pressure manifests itself ana-tomically here sooner than elsewhere. In the earliest stage the lamina cribrosa forms a curve with the concavity forwards instead of passing

Fig. 750.—Cupping of the Disc in Glaucoma.

transversely across the nerve. The nerve-fibres atrophy, partly as the result of pressure upon them in the nerve-head, partly through degenera-tion of the ganglion-cells in the retina from which they spring. The cupping of the disc is, therefore, due partly to a true ectasia and partly to loss of substance. The ectatic element increases as the case advances, so that finally the lamina cribrosa may be pushed back even beyond the level of the sclerotic. The sclera, which then forms the lateral wall of the cup, frequently becomes excavated so that the anterior edge of the scleral foramen forms an overhanging lip, a condition which is familiar in the ophthalmoscopic picture (Figs. 750—752). The nerve-fibres line the cup, more and more becoming atrophied as time advances. As the field of vision shows, the temporal fibres suffer earliest. In early stages degeneration in the nerve-fibres in the trunk of the optic nerve can be demonstrated by the Marchi method. Later

FIG. 751.—CUPPING OF THE DISC IN GLAUCOMA.
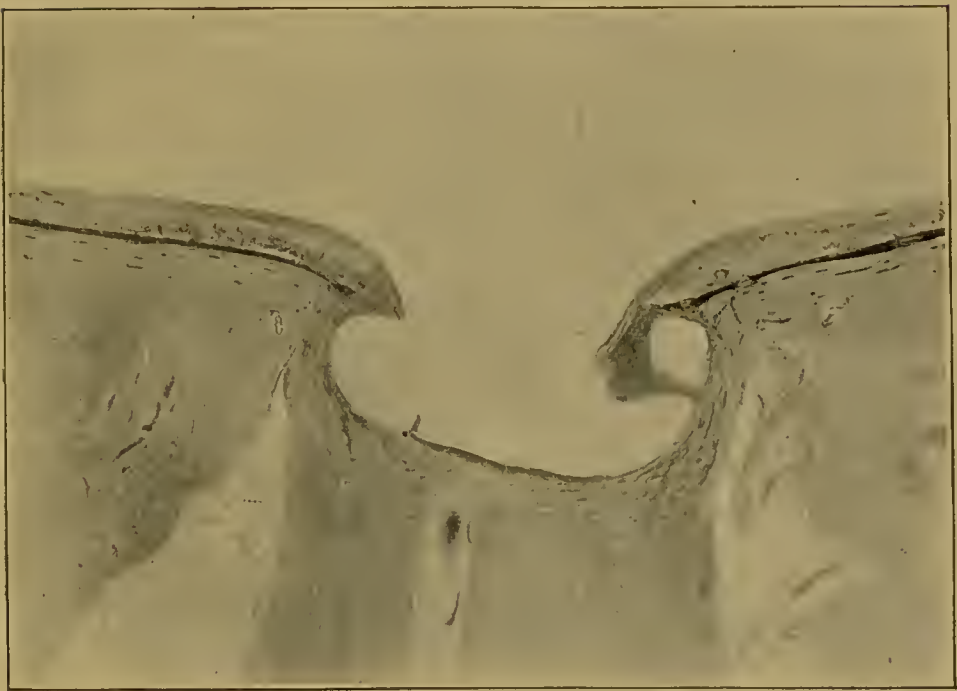
FIG. 752.—CUPPING OF THE DISC IN GLAUCOMA.
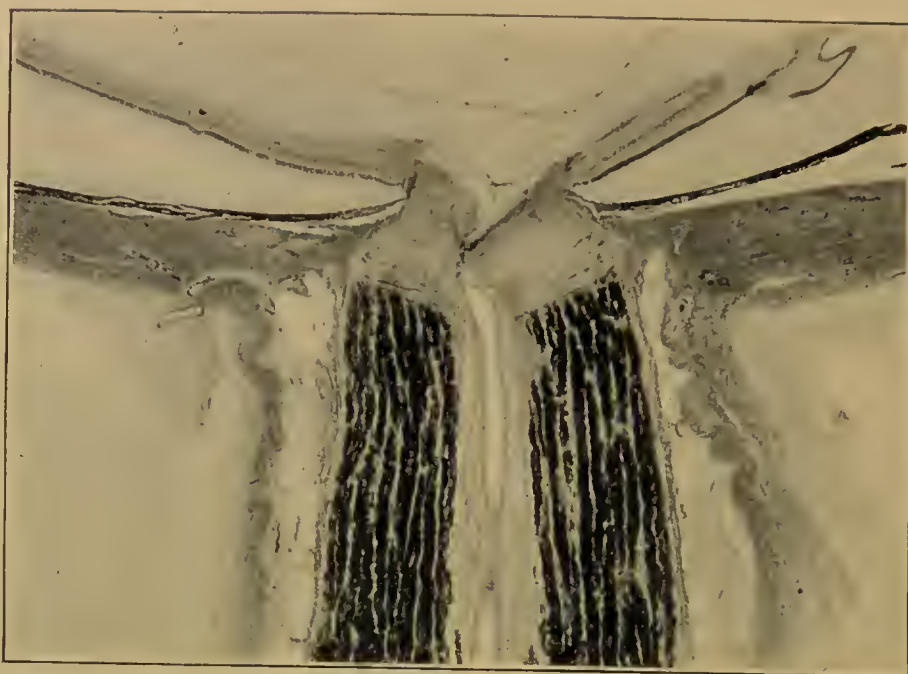
FIG. 753.—NORMAL OPTIC NERVE.
Stained by Weigert's method.
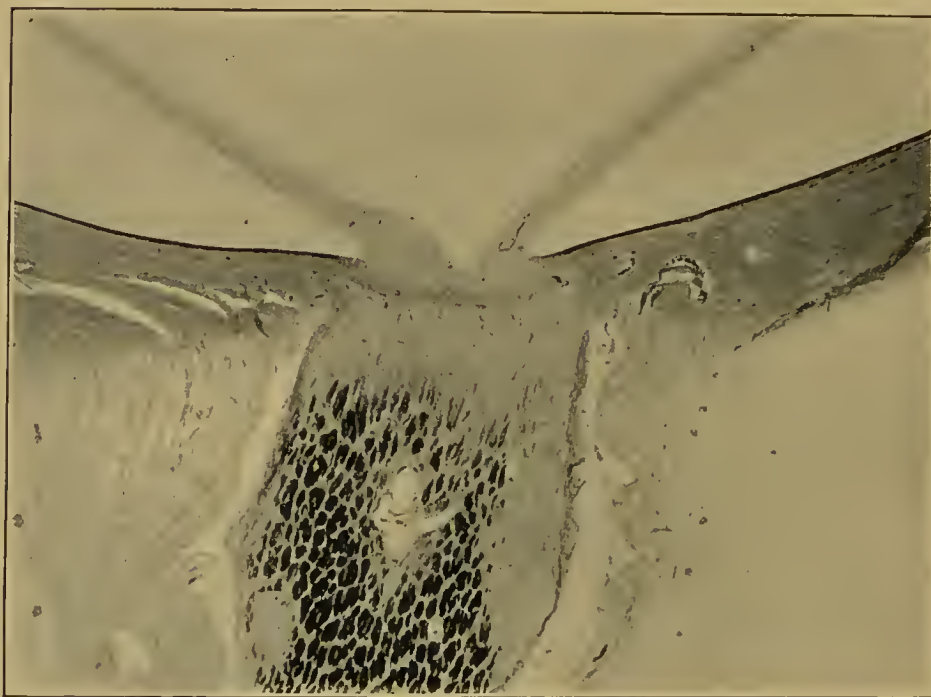
FIG. 754.—OPTIC NERVE IN EARLY GLAUCOMA.
Stained by Weigert's method.

all the fibres have degenerated and the usual appearances of total optic
atrophy (q. v.) are seen.

The general opinion attributes the condition of the optic nerve
entirely to the deleterious effects of prolonged abnormal pressure, as
just described. Schnabel has brought forward the view that there is
also an active neuritic atrophy, as shown by the formation of new
blood-vessels, proliferation of the interstitial connective tissue, etc.
These changes, however, occur as a compensatory process in pure
atrophy. Schnabel considers that the lamina cribrosa is not pressed
back by the increased pressure, but pulled back by the shrinking con-
nective tissue of the atrophic nerve. From a review of the condition
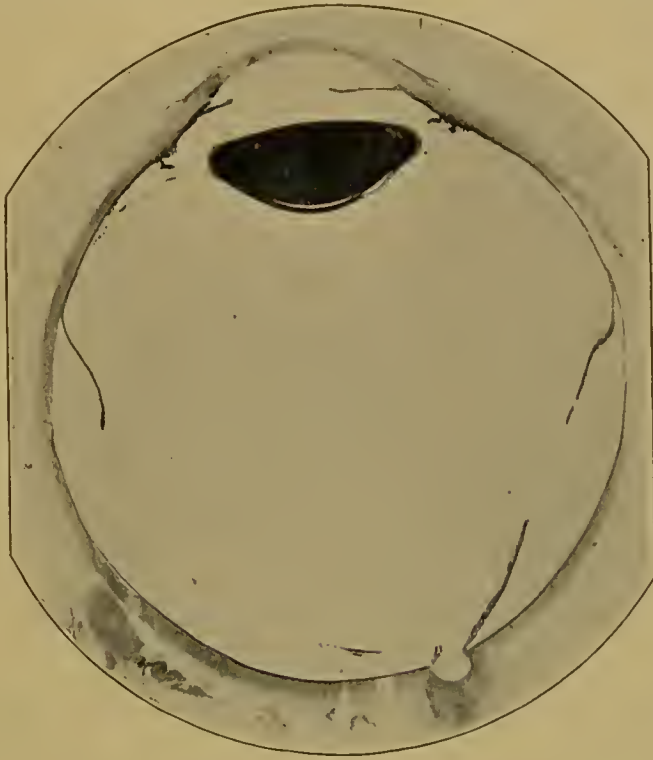
FIG. 755.—GLAUCOMA.
Horizontal section.

in forty-two eyes, he deduces the following sequence of events.
Degeneration of the nerve-fibres, which commences in the intra-scleral
part, leads to the formation of microscopic holes which rapidly enlarge
—cavernous degeneration. The holes coalesce into clefts and irregular
spaces, so that the lamina cribrosa becomes exposed upon the
surface anteriorly. Finally, a single large cavern results—the glauco-
matous excavation. Associated with the cavernous degeneration
there is a condensation degeneration (*Verdichtungsschwund*). It is
probable that in the majority of cases this cavernous degeneration does
not take place, and that it may occur quite independently of the glauco-
matous process. A very marked case has been reported by Schnaudigel.
Cases occur in which the clinical diagnosis between glaucoma and
optic atrophy is extremely difficult; in some of these large cavernous

spaces are found around the central vessels anterior to the lamina cribrosa (Schmidt-Rimpler). The ultimate appearance in this condition is one in which there is a papilliform projection in the floor of the cup, and this is not very uncommon; it has usually been considered a mere variety of the ordinary glaucoma cup (Fig. 751). The exact significance of cavernous degeneration, which has also been observed by Treitel, Deutschmann, Elschnig, and Hummelsheim and Leber, must be left to further research.

The glaucoma cup is, of course, usually filled with vitreous. The amount of connective tissue on the surface of the lamina cribrosa varies enormously. It may be almost absent, or the cup may be filled with new-formed connective tissue. It is probable that this depends primarily on the condition of the normal connective-tissue meniscus (v. Vol. II, p. 656). I have already pointed out that there is a relatively large amount of mesoblastic tissue in this position and around the central vessels near the disc, and that this fact is of considerable importance in my opinion in the pathogenesis of retinitis proliferans (q.v.). Römer has reported a case of chronic nephritis with a glaucomatous excavation which was filled in with connective tissue, strands of which radiated far into the vitreous, and he has called attention to the relationship with retinitis proliferans. The frequent association of retinitis proliferans with vitreous hæmorrhage renders it probable that in these filled in glaucoma cups this factor may be the essential cause. Cases of hæmorrhage into a glaucoma cup are figured by Siebreich and Hartridge.

Intimately related to these cases are those in which papillitis has been associated with glaucoma. The so-called papillitis has been unilateral, and the connection between the two conditions is obscure, as in the neuritic atrophy of Schnabel (cf. Fuchs, Brailey, Elschnig). Bitzos went so far as to state that glaucoma always commences with a papillitis, an obvious error. The case reported by Webster Fox and Brailey was doubtless one of thrombosis of the central vein, and it is likely that this factor may account for the condition generally. Moauro recorded a case of glaucoma in a blind eye with glaucoma and papillitis in the other eye. Three theories have been reviewed by Krukenberg: (1) that of Mooren, that the papillitis is invariably a sign of general disease; this is unlikely owing to the rarity of unilateral neuritis in these diseases; (2) that the cupping of the disc is congenital, as shown to be possible by Kranz and others; (3) that proliferation of tissue, and probably œdema, has occurred in a preformed glaucoma cup. The last view is most probable; there is a pseudo-neuritis due to this cause. That it is not a true neuritis is shown in most cases by the total atrophy of the nerve-fibres.

The effect of prolonged high tension upon the sclerotic is to cause stretching and ectasiæ. If the eye is young the sclera may become equably stretched, and total ectasia occurs (v. infra, " Infantile Glaucoma "). In older eyes the resistance is greater, and only the weakest parts suffer, partial ectasiæ being produced; these may also occur as the result of normal intra-ocular pressure acting upon spots weakened by inflammation, etc. Ciliary and equatorial ectasiæ or

staphylomata occur as the result of glaucoma ; posterior ectasia or staphyloma is, as has been seen, the prominent feature of axial myopia.

Ciliary staphylomata form a bluish bulging in the ciliary region beyond

FIG. 756.—CILIARY STAPHYLOMA.
After Lawson. From a specimen in the
R. L. O. H. Museum.
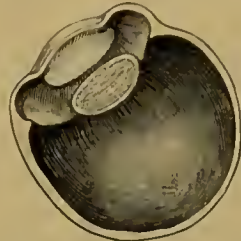
FIG. 757.—INTERCALARY STAPHYLOMA.
After Lawson. From a specimen in the
R. L. O. H. Museum.

the limbus ; they may be small and localised, single or multiple, or annular, surrounding the whole circumference of the cornea. Isolated staphylomata tend to increase in size under the continued pressure, and to become confluent. Anatomical examination shows that there are
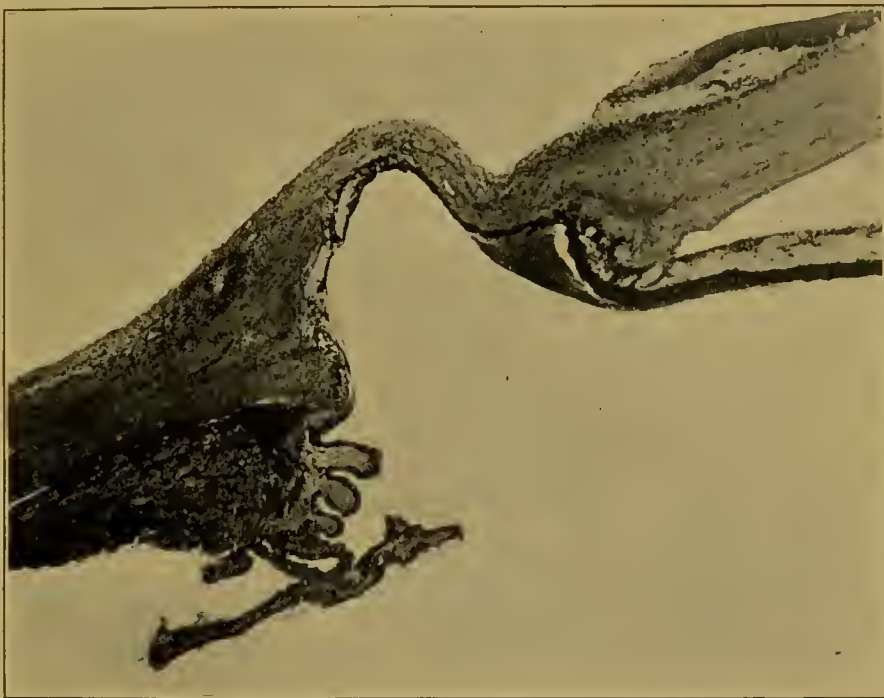
FIG. 758.—INTERCALARY STAPHYLOMA.

two distinct types of ciliary staphyloma—ciliary staphyloma proper and intercalary staphyloma. In *ciliary staphyloma proper* the sclera covering the ciliary body is stretched, so that the ciliary processes are thinned out and extended over the inner surface of the bulging area. In *intercalary staphyloma* it is the part of the sclerotic anterior to the ciliary body which becomes stretched (Fig. 758). It probably seldom,

if ever, arises without previous adhesion of the periphery of the iris to the sclero-corneal junction at this spot, certainly not in glaucoma. It is conceivable that an inherent weakness here might lead to bulging, the iris being pressed forwards secondarily into contact with the ectatic spot, subsequently becoming adherent to it and stretching with it. In glaucoma the iris is already adherent, and it is the adherent area which stretches, probably to a large extent aided by the degeneration of the tissues following the establishment of the synechia. The intercalary staphyloma will therefore have the iris springing from the anterior edge, this representing, not the true base of the iris, but the position of the false angle. At the posterior margin of the staphyloma is the ciliary body. In a pure intercalary staphyloma the ciliary body will be little changed and quite recognisable. It is seldom, however, that a pure intercalary staphyloma is seen. The ciliary staphyloma proper is rather more common, but in the vast majority of cases there is a mixture of the two conditions—i.e. there is ectasia, not only of the intercalary area, but also of the true ciliary area. The distinction is of no clinical, and of little pathological, importance.

Fig. 759.—Equatorial Staphyloma.

After Lawson. From a specimen in the R. L. O. H. Museum.

Equatorial staphyloma is less common. It usually commences in the neighbourhood of a vortex vein, and is therefore generally slightly behind the equator. It is probable that there must be some inherent weakness in the sclerotic, due to scleritis, etc., but this may well be a sequel of glaucoma.

Microscopically, in partial staphylomata the sclerotic is found to be extremely attenuated, forming a thin membrane, over the inner surface of which the very degenerated uvea is stretched, scarcely recognisable but for its pigment.

Priestley Smith.—Glaucoma, London, 1879, 1891. Brailey.—R. L. O. H. Rep., x, 1882. Birnbacher and Czermak.—A. f. O., xxxii, 2, 1886. Birnbacher.—Ein Beiträg zur· Anat. d. Glaucoma acutum, Graz, 1890. Stirling.—R. L. O. H. Rep., xiii, 1893. Berenstein.—A. f. O., li, 1, 1900. E. v. Hippel.—A. f. O., lii, 3, 1901. Ischreyt and Reinhard.—A. f. A., xliii, 1901. Nicolai.—Internat. Ophth. Congress, Utrecht, 1899. Koster Gzn.—A. f. O., xli, 2, 1895. H. Müller.—Gesammelte Schriften, Leipzig, 1872. Schnabel.—A. f. A., xxiv, 1892; Wiener med. Woch., 1900. Schnaudigel.—A. f. O., lix, 2, 1904. Schmidt-Rimpler.—A. f. O., lviii, 3, 1904. Treitel.—A. f. O., xxii, 2, 1876. Deutschmann.—A. f. O., xxv, 3, 1879. Elschnig.—A. f. A., xxxiii, Ergänzungsheft, 1896. Hummelsheim and Leber.—A. f. O., lii, 2, 1901. Römer.—A. f. O., lii, 3, 1901. Hartridge.—T. O. S., xi, 1891. Fuchs.—A. f. O., xxx, 3, 1884. Bitzos.—A. f. O., xxvi, 2, 1880. Webster Fox and Brailey.—R. L. O. H. Rep., x, 1881. Moauro.—Atti d. r. Ass. med.-chir. di Napoli, xlvi. Krukenberg.—K. M. f. A., xxxviii, Beilageheft, 1900. Mooren.—A. f. A., xiii, 1884. Kranz.—Dissertation, Marburg, 1898.

The pathological anatomy of primary glaucoma tends to show that sooner or later the periphery of the iris becomes adherent to the cornea and the filtration angle becomes blocked. It remains, therefore, to discover why the iris becomes apposed to the cornea. Knies attributed it to a circumscribed inflammation of the ligamentum pectinatum and the adjacent tissues, and Birnbacher and Czermak supported this theory. Granting the possibility of such a result from inflammatory changes, it

is rendered improbable from the absence of any cause or sign of true inflammation other than congestion. This is most obvious in the more chronic forms of primary glaucoma, but indicated even in the more acute. For this reason it is well to avoid the term "inflammatory" in connection with glaucoma, and to replace it by "congestive," with Priestley Smith. It need scarcely be mentioned that a narrow peripheral anterior synechia is quite invisible clinically, the affected part being hidden under the sclerotic.

The most probable theory as to the cause of the obstruction to filtration in primary glaucoma is that put forward by Priestley Smith in 1879, and since elaborated by careful measurements. He attributes it to disproportion between the size of the lens and the size of the eye. The following is a *résumé* of his investigations and the deductions based upon them.

Predisposing causes.—Priestley Smith points out the following
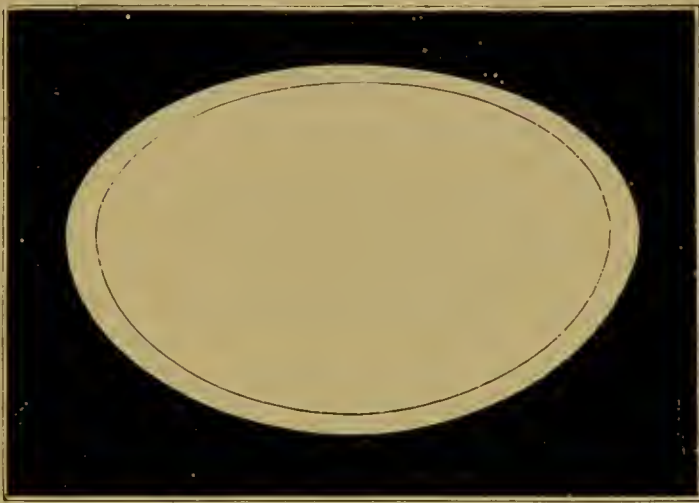
FIG. 760.—SIZE OF THE LENS.
Priestley Smith, T. O. S., iii. Relative sizes of average healthy lens at 25 and 65 years of age.

facts: (1) The size of the lens increases throughout life; (2) the liability to primary glaucoma increases throughout life; (3) the liability to primary glaucoma is greatest in eyes of exceptionally small size; (4) a disproportion between the size of the lens and the size of the globe can be demonstrated in some eyes blinded by primary glaucoma.

Growth and size of the lens.—In order to ascertain whether the relation of the lens to the surrounding parts varies at different periods of adult life Priestley Smith examined 156 lenses from the dead subject, taken in equal numbers from the six decades of life between twenty and eighty, and in smaller number between eighty and ninety. Each lens was accurately weighed, and its volume was measured by a specially devised apparatus (Fig. 694). The results show that the lens, so long as it remains healthy, increases in weight and in volume throughout life. During the forty years between twenty-five and sixty-

five it adds about one third to its weight, one third to its volume, and one tenth to its diameters.   The specific gravity shows no decided change.   Lenses which are becoming cataractous are generally smaller than healthy lenses belonging to the same period of life.

The explanation of these facts is to be found in the development of the lens.   It is derived from the cuticular epiblast, but its cells, unlike those of the cuticle, are not cast off as they grow old ; they are laid down layer upon layer within a closed capsule, the younger fibres surrounding the older.   Hence, in spite of the shrinking of the older cells, which form the nucleus, the growth of the lens does not cease with that of the rest of the body, but is continuous in the absence of some intercurrent morbid process.   In advanced life the process of growth often fails ; then the shrinking nucleus tends to separate from the softer cortex, and senile cataract begins (Becker, Priestley Smith).   The lens with incipient cataract is, therefore, usually smaller than the healthy lens of the same age.   As the cortex swells this early stage gives place to one in which the lens is larger than normal.

The structures which surround the lens attain their full dimensions at the commencement of adult life or perhaps earlier, for the diameter of the cornea increases little, if at all, after the fifth year (*v. infra*). Hence, as age advances the lens steadily encroaches upon the surrounding space, its margin comes into closer relation with the ciliary processes, and the whole circumlental space is diminished.   This fact accounts, too, for the diminution in depth of the anterior chamber in old age, for there is no proof that the lens advances bodily.

Liability to primary glaucoma in relation to age.—Priestley Smith collected accurate data concerning 1000 cases of primary glaucoma ; they were tabulated according to sex, age of incidence, and type of disease, whether chronic, subacute, or acute.   The results as to *frequency* were : (1) Primary glaucoma is extremely rare in childhood and youth ; not 1 per cent. of cases begins earlier than the twentieth year ; (2) the frequency increases, slowly at first, more rapidly later, in each decade until about the sixtieth year ; between sixty and seventy it is about as frequent as between fifty and sixty ; after seventy its frequency diminishes ; (3) cases beginning after fifty are about twice as numerous as those beginning before fifty—679 to 321 per 1000 ; (4) females are rather more affected than males—569 to 431 per 1000 ; (5) the chronic, non-congestive form is rather commoner in males than in females—253 to 223 per 1000 ; (6) the acute and subacute, congestive forms are much commoner in females than in males—346 to 178 per 1000.

As regards *liability* : (1) The liability to primary glaucoma is extremely slight in childhood and youth as compared with later periods of life ; thus at fifteen it is at least one hundred times less than at sixty-five ; (2) it continually increases up to and during the seventh decade ; between sixty and seventy it is more than twice as great as between forty and fifty ; (3) after seventy the liability declines considerably, but the statistics are probably less reliable ; (4) the liability of females is greater than that of males in the ratio of about 6 : 5 ; (5) the greater liability of females pertains to the whole of life, but the data before thirty and after seventy are too few to justify generalisation ; (6) the
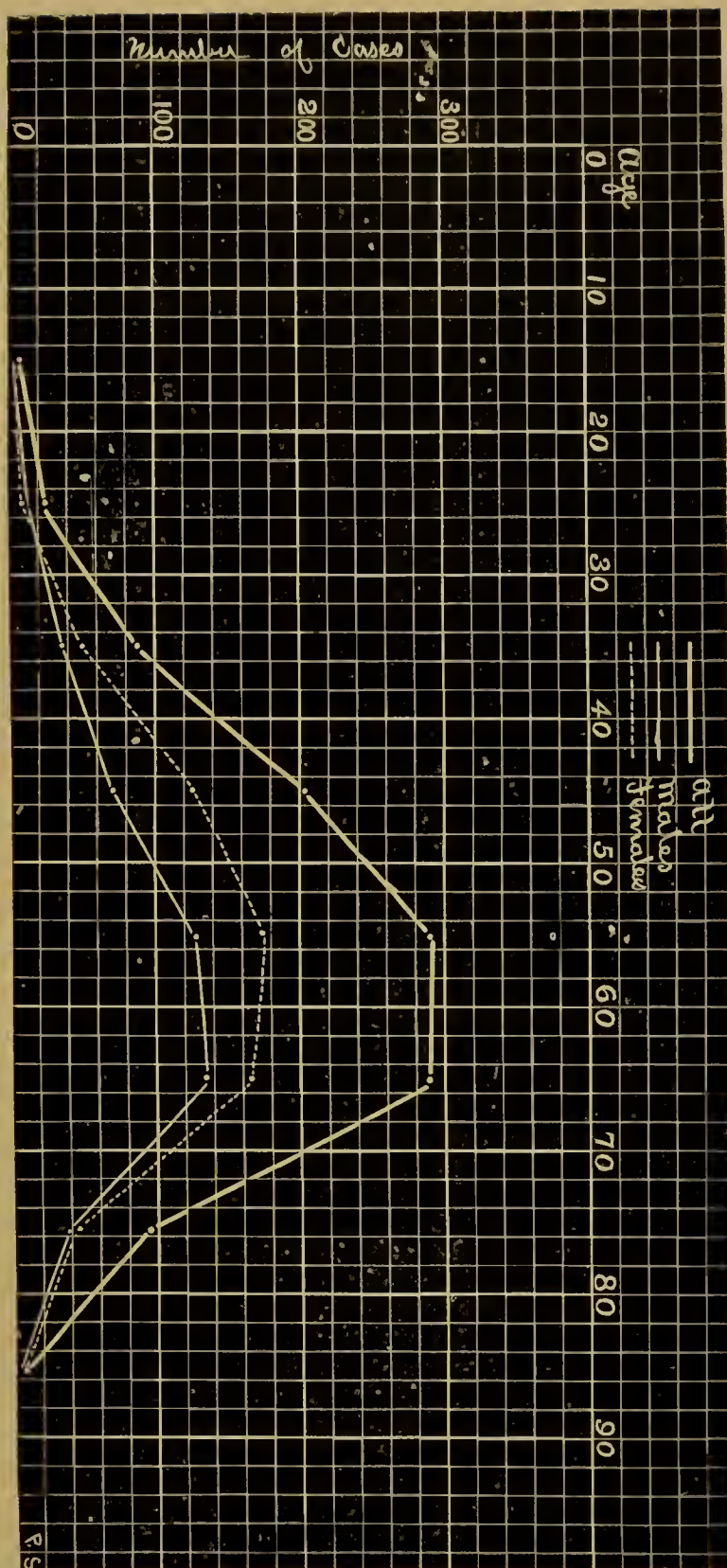
Fig. 761.—Frequency of Primary Glaucoma at different Life-periods.
From Priestley Smith. Distribution of 1000 cases.
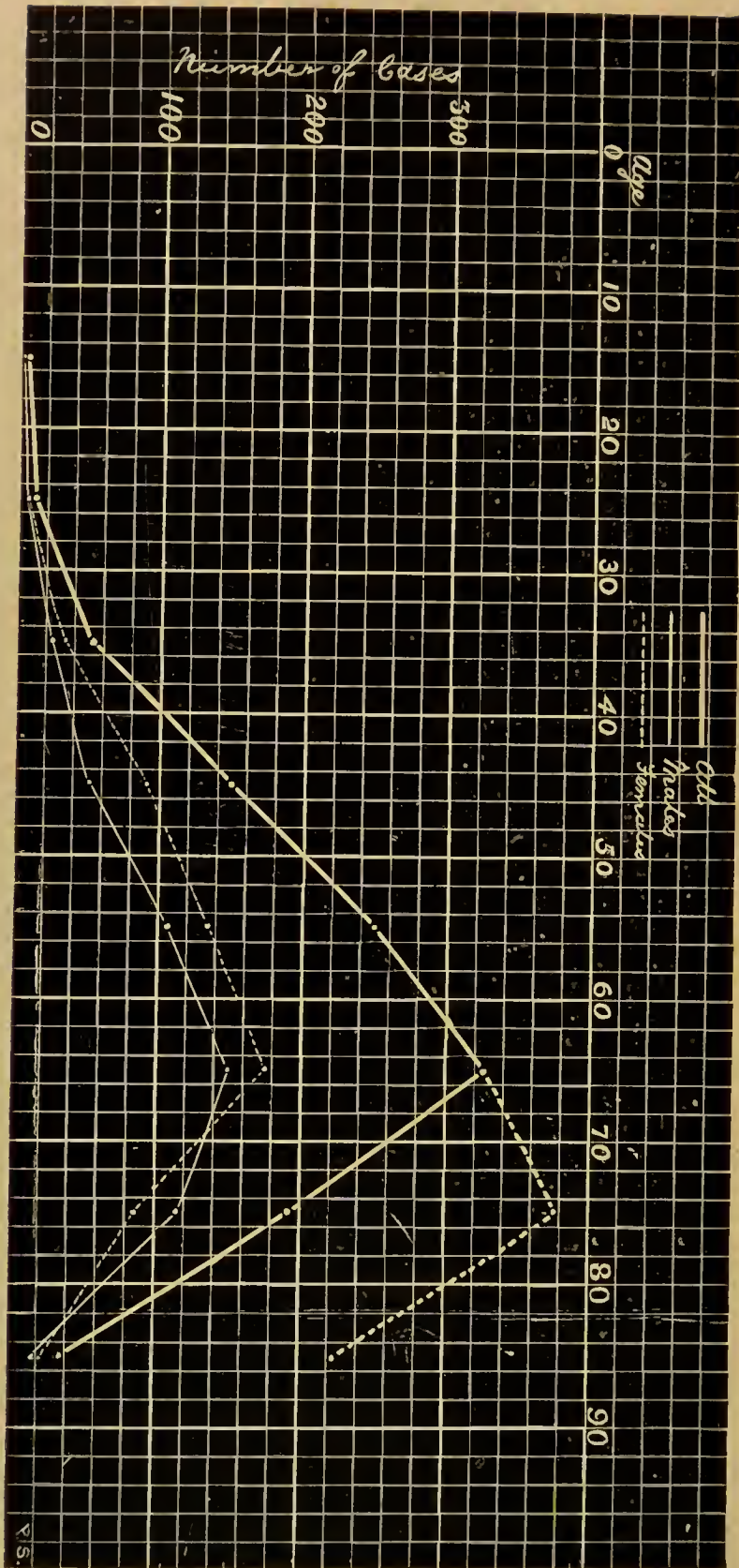
FIG. 762.—LIABILITY TO PRIMARY GLAUCOMA AT DIFFERENT LIFE-PERIODS.
From Priestley Smith. The same 1000 cases distributed as though persons
of all ages and both sexes were equally numerous.

greater liability of females relates very markedly to the congestive forms of the disease, not to the non-congestive.

Growth and size of the cornea.—It is a matter of common observation that patients with primary glaucoma have small corneæ, a fact which accentuates the difficulties of iridectomy. Priestley Smith has shown that there is a distinct relationship between the size of the cornea and the size of the globe. By means of the keratometer he measured one thousand corneæ, belonging in equal number to the two sexes, and representing all periods of life from five to ninety years of age. He arrived at the following deductions with regard to healthy eyes : (1) The mean horizontal diameter in persons between five and ninety is 11·6 mm.; variations beyond 11 mm. and 12 mm. are present in about 5 per cent.; (2) the average increases little, if at all, after five years of age ; (3) there is perhaps a slight diminution in the size of the cornea after forty ; (4) the average appears to be slightly greater in males than in females ; (5) the average is the same in all states of refraction—an unexpected result ; (6) there is very rarely any difference between the two eyes of the same individual, irrespective of refraction.

Priestley Smith examined fifty-one males and sixty-one females suffering in one eye or both from primary glaucoma. Their average age was fifty-seven. The number of eyes was 216, of which 169 were glaucomatous and 47 healthy. The following are the general results : (1) The mean horizontal diameter of the cornea measures 11·17 mm. ; (2) the percentage of unusually small corneæ—*i. e.* 10·5 mm. or less—is much greater in the glaucoma group than in the healthy group— 22·69 per cent. : 1·70 per cent., or, excluding healthy eyes of persons under forty, 22·69 per cent. : 3·79 per cent. ; (3) a horizontal diameter of 10 mm. was found nine times—*i. e.* in 4·17 per cent.

The next point was to examine the relative sizes of cornea and globe. In twenty-five non-glaucomatous eyeballs it was found that : (1) there is no constant proportion between the two diameters of the cornea, or between the several diameters of the globe, or between the diameters of the cornea and those of the globe ; (2) there is on an average a fairly regular proportion in these respects ; thus, the horizontal diameter of the cornea is somewhat larger than its vertical diameter ; the difference is smaller in these measurements for the globe ; these diameters of the globe usually vary directly with the corresponding diameters of the cornea.

It is clear, therefore, that small corneæ belong, as a rule, to small globes, and small eyes are more liable to primary glaucoma than large ones (*cf.* Bader, Brugsch Bey). Direct measurements on fourteen eyes blinded by primary glaucoma confirm these conclusions. Comparing the averages, the results are :

| | Cornea. | | Globe. | | Antero- |
	Horizontal.	Vertical.	Horizontal.	Vertical.	posterior.
Healthy	11·6	11·0	24·4	24·0	24·8
Glaucomatous	11·1	10·3	23·3	22·9	23·4

It remains to show whether the normal relative size of the lens was maintained in these small eyes. If they contain proportionately small lenses their special liability to glaucoma cannot be due to a faulty

relation between the lens and its surroundings. The question is difficult, since not only are the specimens rare, but each lens must be considered in relation to the age of the patient as well as to the size of the globe.

Considering extreme cases, the lens is usually disproportionately large in microphthalmia (q. v.). Microphthalmic eyes with transparent lenses are very prone to glaucoma (cf. Kundrat, Treacher Collins, and others). Priestley Smith found that the size of the lens bore no fixed proportion to the size of the globe even at the same period of life ; in his glaucoma cases there were several instances of a large lens in a small eye, but the evidence of a general rule cannot be considered conclusive.

Refraction.—Statistics show that hypermetropia is the commonest condition of refraction in eyes affected with primary glaucoma, and it has therefore been assumed that there is an essential connection between the two conditions. This assumption is not altogether justified. At the time of life when primary glaucoma chiefly occurs hypermetropia is very common. The emmetropic eye tends to become somewhat hypermetropic after the fiftieth year, so that by the eightieth year there is frequently an acquired hypermetropia of 2—4 D (Donders). Moreover, the special liability of small eyes does not prove special liability of hypermetropic eyes, for small eyes are not necessarily hypermetropic, nor *vice-versâ*. Priestley Smith has shown that small corneæ are not specially associated with hypermetropia ; of 49 small corneæ 21 were associated with hypermetropia, 18 with emmetropia, and 4 with myopia. *Per contra*, hypermetropic eyes have not as a rule smaller corneæ than emmetropic or myopic. It is the *small eye* which is specially liable to glaucoma. The preponderance of hypermetropia in glaucoma is not very marked ; in 164 eyes 74 (45·1 per cent.) were hypermetropic, 67 (40·9 per cent.) emmetropic, and 23 (14 per cent.) myopic (Priestley Smith). In a much larger series of cases Kryoukoff found about the same proportion.

On other grounds, however, it may be urged that hypermetropia is a predisposing cause of glaucoma. The ciliary body is usually more prominent in the direction of the lens in these eyes. Whether excessive accommodation is an exciting cause is open to dispute (*v. infra*).

Race.—Certain races show a special liability to primary glaucoma. Brugsch Bey found a higher percentage amongst Egyptians than is common in European clinics. Moura noted a much higher percentage among negroes than among whites in Rio de Janeiro. Whether Jews are particularly predisposed is uncertain.

Exciting causes.—In an eye predisposed to primary glaucoma owing to the causes already considered, any disturbance which further diminishes the circumlental space or displaces the lens and iris forwards will probably induce an attack. Clinical observation shows that some such mechanism is often at work. The following are some principal factors.

Dilatation of the pupil.—It is well known that atropin and other mydriatics often precipitate an acute attack of glaucoma. It is easy to understand how the folding of the base of the iris may suffice to completely obstruct an already dangerously narrowed filtration angle.

Congestion and inflammation of the uveal tract.—The common ante-

cedents of glaucomatous attacks are conditions which disturb the circulation and tend to cause congestion of the venous system—*e. g.* cold, constipation, sleeplessness, fatigue, bronchitis, indigestion, etc.; and the influences which tend most to relieve the milder attacks are pre-eminently those which relieve congestion—*e. g.* warmth, rest, sleep, purgation, etc.

Exudations from the uveal tract are sometimes concerned in the outbreak of glaucoma. If there is an undoubted iridocyclitis, that alone may suffice to explain the condition, but it is probable that a much slighter inflammation of the iris or ciliary body may induce a true glaucoma in an eye already predisposed than would suffice to raise the tension in an otherwise normal eye.

It has already been stated that great importance has been ascribed to peri- and endo-vascular changes in the vortex veins (Birnbacher and Czermak). It has been pointed out that these changes are not very obvious (Priestley Smith, Stirling), and that they are the changes which are not infrequent in old age. Whilst admitting these facts, and that a glaucoma induced by blockage of the venæ vorticosæ would scarcely be relieved by eserin or iridectomy, yet it is possible that a very slight obstruction to the venous outflow might suffice to bring on an attack in an eye already in a perilous condition. Even so, however, the condition is to be regarded as a predisposing rather than an exciting cause.

It is astonishing how slight may be the apparent exciting cause—*e. g.* a foreign body on the cornea, a trivial blow, or one not implicating the eye itself, operation upon the opposite eye, etc. It is futile to attempt to elucidate these cases minutely, but they all point to some general condition, nervous or otherwise, which modifies the blood-circulation in the eye, for it is hardly conceivable in the absence of a true secretion that any other mechanism could produce the result.

Patients of the age at which the primary glaucoma is commonest frequently have degenerative vascular conditions due to some diathesis, gouty or otherwise, or to some unknown cause. Associated with these anatomical defects there is often abnormally high blood-pressure. Now, it has been shown conclusively in the previous chapter that there is no reason to suppose that mere increased blood-pressure can cause permanent increase of intra-ocular pressure. The effect is transient, the increased production of lymph being compensated by increased outflow. Indeed, it is possible that the greater flushing of the paths of filtration may open them up mechanically and render them abnormally permeable, but the actual effect produced must clearly depend entirely upon the exact anatomical conditions and the ability of the filtration paths to accommodate themselves to the new conditions. The degenerate condition of the vessels may, however, easily lead to hæmorrhages, venous or arterial, small or large. It is difficult here to distinguish between hæmorrhage causing glaucoma and that resulting from it, for that both occur is beyond dispute. In the case of comparatively large hæmorrhages the sudden increase of fluid-content in the post-lental spaces of the eye doubtless directly causes increased tension, which is maintained by the consequent advance of the lens

and iris and the blocking of the angle thereby induced. It is scarcely probable that this is the rationale of the glaucoma in the case of less severe hæmorrhages. Here it is more likely that the highly albuminous plasma of the extravasated blood mingles with the normal lymph and results in a fluid which filters with great difficulty.

Displacement of the lens.—It is probable that a variety of conditions other than those already considered may cause some slight forward displacement of the lens, especially, perhaps, changes in the constitution of the lymph in the vitreous, brought about by changes in the nutrition of the choroid, retina, or vitreous, of which little or nothing is known.

Again, the condition of the circumlental space in old eyes is largely a matter of conjecture. What, for example, is the condition of the ciliary muscle and suspensory ligament after presbyopia has set in? It is probable that the ciliary muscle continues to contract during accommodation, though the lens remains impassive. Such contractions may be expected to slacken the zonule, so that the lens becomes more movable than during accommodation earlier in life. An abnormal slackness of the zonule has also been ascribed to degenerative changes (Snellen).

The supposed association of glaucoma with hypermetropia has led to the theory that excessive accommodation is an exciting cause. It has been pointed out that the *rôle* of hypermetropia has been exaggerated, but even so accommodative efforts may be expected to have a deleterious influence, especially in the presence of congestion of the ciliary body or slight inflammation. One is familiar with the extreme importance of keeping the iris and ciliary body at rest in cases of iritis or cyclitis, and it is not unlikely that contraction of the ciliary muscle may increase congestion. In the irritated condition of the ciliary body which must occur in some cases of glaucoma the ciliary muscle is probably in a condition of tonic contraction. There is no reason to assume that the ciliary muscle ceases to contract after the onset of presbyopia, so that any effect of this nature will apply equally in these cases. Priestley Smith has well remarked that the position assumed in reading and near work often conduces to venous congestion of the head.

Apart from actual advance of the lens increase in size of the lens has already received attention, but it may be added that the swelling of the lens in the second stage of cataract may suffice to block the narrowed circumlental space of an eye predisposed to glaucoma.

Sex.—Priestley Smith has shown that while the liability to the simple non-congestive form of primary glaucoma is about equal in the two sexes, women are much more prone than men to congestive exacerbations, or even to anticipate the onset of the chronic disease by attacks of the congestive type. This special tendency may be reasonably referred to the greater instability of their vasomotor systems, and particularly to disturbances of circulation which originate in the generative organs—*e. g.* disorders of menstruation, especially at the climacteric.

The rationale of iridectomy, etc.—It will be more convenient to consider here the rationale of iridectomy and other operations for the

relief of glaucoma than in the more logical position under " Wounds of the Eye."

It has been mentioned that iridectomy was introduced by v. Graefe on empirical grounds. Now that the pathology of glaucoma is better understood it is possible to comprehend more or less thoroughly the mechanism of its action when successful and the causes of failure when unsuccessful. Statistics show that iridectomy is most successful in acute cases of primary glaucoma. Here the condition is one of apposition of the periphery of the iris to the cornea, with very little gumming together of the apposed surfaces. It has been shown that when the iris is torn away, as in iridectomy for glaucoma (" iridecto-

FIG. 763.—IRIDECTOMY FOR GLAUCOMA.
From a photograph by Coats. The iridectomy has failed to open up the occluded angle of the anterior chamber.

medialysis "), the rupture of the iris tissue takes place at the extreme periphery of its base; in other words, the most peripheral iridectomy is obtained by this method. Now, in acute glaucoma mere apposition of the iris to the cornea or even slight adhesion will be quite insufficient to prevent the iris tearing away in this situation. In this manner the filtration angle is re-opened, the congestion of the ciliary processes, etc., quickly subsides, and normal tension is restored and maintained.

It has already been shown that the longer the iris is apposed to the cornea the greater is the adhesion, and the more widespread it is likely to become (v. Vol. I, p. 404). It has been shown that the knitting together of iris and cornea is so intimate that it is impossible to imagine that in these cases the iris will tear away in any other position than at the false angle—i. e. at the anterior border of the adhesion. This will totally fail to re-open the filtration angle, and the glaucomatous con-

dition is not relieved. The object of the peripheral, scleral incision in iridectomy for glaucoma is to incise the actual site of adhesion, and if possible to attack the true angle and the canal of Schlemm. Treacher Collins has found from a careful examination of iridectomised eyes that it is extremely rare for the section to pass through the ligamentum pectinatum, and that the canal of Schlemm invariably escapes. He found that the corneo-scleral incision was always oblique, so that the extent of the external wound afforded only an imperfect criterion of the position and extent of the internal wound. It is not surprising therefore that late iridectomy in chronic glaucoma fails to relieve the abnormal tension. There are cases, however, in which it succeeds, and many of these show operative results which are otherwise surgically reprehensible, such as the formation of cystoid cicatrices, etc. It was

FIG. 764.—A FILTERING SCAR.
From Priestley Smith. Tangenital section. Open channels were seen in every section.

long ago advanced by de Wecker that the operation restores permanent filtration either by creating a permeable cicatrix or by establishing communication with the veins. Priestley Smith and Treacher Collins have shown that microscopic fistulæ do actually occur and can be demonstrated in some iridectomy scars. The former showed that in some instances pressure on the globe with the finger, weeks after the operation, will produce visible extrusion of fluid into the conjunctiva, and a corresponding slackening of the globe. de Wecker relates the case of a glaucomatous patient who was in the habit of relieving the slight recurrences to which he was liable after iridectomy by pressing the eyeball with his fingers. It is true that the intact iris tissue is impermeable to fluid, and that the pigment epithelium is chiefly responsible. In old peripheral anterior synechiæ and in cystoid cicatrices the iris atrophies, but the last element to disappear—and that

never entirely—is the epithelium. Hence even the presence of a cystoid cicatrix may fail to relieve the tension, though it has been advocated that a deliberate attempt should be made to obtain incarceration of the iris (Bader, Herbert). In rare cases the scar is very thin, the epithelium is almost wholly destroyed, and efficient filtration results. Unfortunately, no means are known of insuring this result with safety. In non-glaucomatous eyes experiment has shown that iridectomy tends to diminish, if anything, the filtration of lymph. The conditions which obtain in the glaucomatous eye are, however, very different. Here the raised tension tends to open up every available channel.

The chief causes of failure of iridectomy to relieve tension have already been mentioned incidentally. Reference may again be made to wound of the lens during the operation, failure of the lens to retract and the anterior chamber to reform after the operation, etc.

FIG. 765.—CYSTOID CICATRIX.
Treacher Collins, R. L. O. H. Rep., xiii.   From a case by Bader.

Sclerotomy aims at opening the filtration angle and canal of Schlemm in the same manner as the peripheral section of iridectomy. The reasons of failure are similar. It is unnecessary here to enter into the disadvantages of sclerotomy as compared with iridectomy.

INFANTILE GLAUCOMA (BUPHTHALMIA, HYDROPHTHALMIA).

Buphthalmus or ox-eye was the term used by early writers for a variety of conditions, including, probably, exophthalmos, anterior staphylomata of various kinds, etc. It should be reserved for the type of case which is about to be described. The first approximately complete description is found in the treatise of Saint-Yves (1722). A good description is given by Mackenzie (1830), but he displays the ignorance of the period on the subject in the number of his subdivisions—hydropsy of the aqueous, of the vitreous, of the two chambers, subsclerotic and subchoroidal hydropsy. Sichel (1852) admits only general hydro-

phthalmia, pointing out that anterior hydrophthalmia is only pellucid
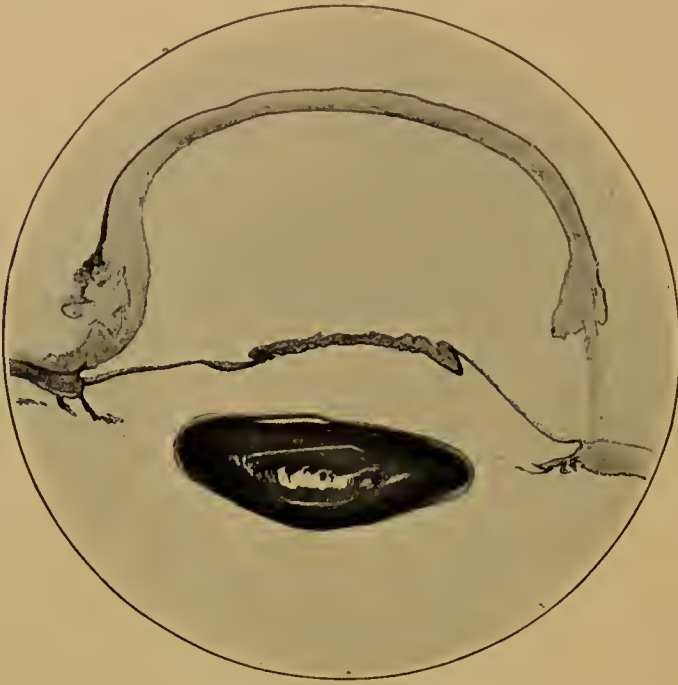
FIG. 766.—Buphthalmia.
From a photograph by Lister.

FIG. 767.—Buphthalmia.
From a photograph by Lister.

corneal staphyloma, and posterior hydrophthalmia subchoroidal
hydropsy or detachment of the retina. Mauthner (1867) first pro-

claimed the glaucomatous nature of buphthalmia, and this view has since received ample confirmation.

Clinically, the most striking feature in buphthalmia is the size of the cornea, which has given rise to the term " magalocornea." It may be clear or dull, opalescent or bluish. The anterior chamber is very deep, the media clear. The distension of the globe is marked by more or less proptosis and by the blue colour of the sclerotic, especially near the limbus, due to thinning. Sometimes there is nystagmus.

The globe is much enlarged, usually oval and elongated, though the plasticity of the young tunics is shown by an unusual increase in diameter of the corneal base. The mean dimensions of twenty eyes give the following results (Gros) :

	Maximum (Schiess-Gemuseus).	Mean.	Normal (Merkel).
Antero-posterior	38·8 mm.	32 mm.	24·3 mm.
Vertical	28·6 ,,	26 ,,	23·6 ,,

The cornea is hemispherical or globular. In twenty cases the minimum horizontal diameter was 12 mm., the maximum 23·5 mm., the mean 16 mm. (Gros), as compared with 11·6 mm. of the normal adult (Merkel). These measurements can only be approximate, since the periphery is often opaque. The cornea is thinned, especially at the periphery. Gros gives the following measurements :

	Minimum.	Maximum.	Mean.	Normal.
Centre	0·28 mm.	1·27 mm.	0·67 mm (12 cases)	0·90 mm.
Periphery	0·20 ,,	0·75 ,,	0·47 ,, (8 ,,)	1·10 ,,

The anterior chamber is very deep ; Grahamer records a unilateral case in which it is said to have been seven or eight times as deep as on the normal side, but this is probably inaccurate. Of ten cases in which careful measurements were made the maximum depth was 12·8 mm. (Schiess-Gemuseus), minimum 3·0 mm. (Dürr and Schlegtendal), mean 6·3 mm. (Gros), normal 2·6 mm. (Merkel).

The iris shows no signs of inflammation. It is usually flat, rarely infundibuliform. The colour shows little abnormal, though the pattern is not so sharply defined as it should be and the colour is not so brilliant. Iridodonesis is common, owing to the lack of proper support from the lens. The pupil is round, usually slightly dilated, rarely much contracted (Dürr and Schlegtendal), or dilated (9 mm., Brunhuber). The pupil reacts badly to light even when vision is fairly well maintained, probably owing to the atrophic condition of the iris. Mydriatics, which should be used with caution, usually cause dilatation. Associated congenital anomalies of the iris have been described—coloboma (Gallenga, E. v. Hippel), corectopia (Kessler, Mayerhausen, Warlomont) ; aniridia (Brunhuber, Pflüger, Cabannès, Venneman) has probably led to a mistaken diagnosis of buphthalmia owing to the apparent increase in depth of the anterior chamber in these cases.

The lens is generally clear, though after the nutrition of the eye begins to suffer in the later stages it frequently becomes cataractous. The lens, in contrast with other parts of the eye, is smaller than normal (Fuchs). The mean diameter in five cases was 6·8 mm. (Gros), as com-

pared with the normal 9 mm. (Merkel). The antero-posterior diameter is also reduced, and the lens appears somewhat spindle-shaped in meridional section, for the same reason as in anterior staphyloma, viz. the stretching of the suspensory ligament by the expansion of the ciliary ring. This tension of the zonule may lead to rupture and dislocation of the lens, which may be partial or complete. More characteristic of buphthalmia, and of considerable clinical importance, is the backward displacement of the lens. This is not only relative to the cornea, due to the deepening of the anterior chamber, but is real as to the retina, and is due to slight displacement backwards of the origin of the suspensory ligament in the ciliary body, brought about by stretching.

Ophthalmoscopic examination shows that the media are usually quite clear. The retina and choroid appear normal in the early stages, and any disease in these membranes must be regarded as independent of the buphthalmic condition. Subjective signs of diminished retinal sensibility are not wanting, however, at this period. There is generally contraction of the field of vision, and it is interesting to note that this is analogous in kind with that found in glaucoma. Owing to the plasticity of the infantile globe the retina does not suffer so soon as in glaucoma of adults, and progresses more slowly. Fuchs suggests that the greater length of the retinal vessels on the temporal side causes this part of the retina to suffer first. Though contraction usually manifests itself first in the nasal field, it is sometimes concentric. In the later stages the retina shows objective signs of disease. Pigment spots or plaques appear, and detachment may occur, though it is rare in the absence of surgical interference.

The optic disc is cupped, as was first pointed out by Mauthner and Arnold. The appearances are the same as in adult glaucoma, but the variations in size of the vessels and arterial pulsation are less commonly observed. Optic atrophy follows as the case progresses. Posterior staphyloma is infrequent, though the myopic condition may be met with (Kalt).

The condition of the refraction is of extreme interest. Considering the increased length of the globe, it might be anticipated that axial myopia would be the rule, but it is by no means invariable. Warlomont described a case of bilateral buphthalmia in a boy, æt. 13, with slight myopia in one eye and emmetropia in the other associated with fair vision (2/3). The possibility of emmetropia or even hypermetropia is explained by three causes: (1) the flattening of the cornea ; (2) the displacement backwards of the lens ; (3) the flattening of the lens. For the same reasons when myopia is present it is less marked than might be anticipated ; myopia of − 15 D or − 16 D (Dehenne) is rare, that of − 1 D to − 7 D relatively common, and also distinctly more frequent than emmetropia or hypermetropia.

Astigmatism is common, and in contrast with adult glaucoma is usually according to the rule—i. e. the horizontal meridian is the more hypermetropic. This is most reasonably explained by the effect of pressure of the lids upon the plastic globe. Astigmatism against the rule has been recorded (e. g. Rochon-Duvigneaud). Irregular astigmatism, as might be expected, is not uncommon in the later stages.

Even with proper correction of the refraction the visual acuity is generally far below the normal.

The intra-ocular tension is raised, and it must be accepted that this is the fundamental cause of the condition. The tension probably never reaches the level met with in adult glaucoma, owing to the lack of rigidity of the sclerotic in early life.

The progress of the disease is slow and probably always dates from birth or before. Owing to its insidious nature, cases rarely come under observation until the condition is fully established. In 45 cases collected by Gros buphthalmia was present at birth or during the first week in 27, in the first year in 6, from the first to the third year in 8, at eight years in 2, and at fourteen years in 2 (Grahamer, Derby).

FIG. 768.   FIG. 769.

FIGS. 768 AND 769.—CORNEA IN BUPHTHALMIA.
Fig. 768.—Central part.   Fig. 769.—Periphery.

Buphthalmia is usually bilateral, and no predilection for one side more than the other can be made out. In 116 cases, 71 were boys, 45 girls, 74 were bilateral, 42 unilateral; in 41 of the latter the right eye was affected in 20, the left in 21. Gros found 8 cases only amongst 12,000 patients of the ophthalmic clinic at the Hôtel-Dieu from 1894 to 1896.

The influence of heredity is well marked. Direct inheritance is rare—Argyll Robertson, in a mother and three children; Venneman, in a mother and son. Arnold, in sixteen cases collected by Haab, failed to find any similar complaint in any of the ancestors. Buphthalmia is essentially a family disease: Jüngken, 7 brothers, 2 sisters being normal; v. Muralt, 2 brothers and a sister; Derby, 3 brothers and a sister, 2 other brothers and a sister being blind; also 2 children in a family of

which the father and 4 other children were blind ; Streatfield, 2 sisters; Rampoldi, 3 sisters ; Gallenga, 6 cases in a collection of 50 ; Dürr and Schlegtendal, 2 brothers and a sister ; Angelucci, 3 sons of a mother with exophthalmic goître ; Johnson, 3 children, 3 older ones being sound ; Reis, 3 brothers.   Pflüger recorded a family in which the mother had bilateral aniridia, a son congenital phthisis bulbi, a daughter bilateral aniridia, and a son bilateral aniridia with buphthalmia (?).

Consanguinity of parents has been noticed in several cases, and stress is laid upon this point by Zahn.   Laqueur found five cases of children of consanguineous marriages amongst thirteen cases of buphthalmia.   Zahn puts the percentage at roughly 10, and this is probably nearer the mark.   Examples are also given by Reis and others.

Apart from aniridia, corectopia, and coloboma of the iris other congenital anomalies associated with buphthalmia have been lenticonus posterior (Pergens), bilateral glioma retinæ (Pergens), alopecia congenita (Pincus, Lezius), and plexiform neuroma (Sachsalber, Snell and Treacher Collins, Verhoeff, Treacher Collins and Rayner Batten).

Pathological anatomy.—The shape and size of the cornea have already been described.   The centre is often of normal thickness and shows no pathological changes ; the periphery is always much thinned, and is often cellular and vascularised (Figs. 768, 769).   There can be no doubt that the weak sclero-corneal junction, the intercalary region, is the weakest part, which gives way before increased intra-ocular pressure, so that the cornea proper is displaced bodily forwards. At the same time the base circle becomes stretched, some flattening of the cornea being the result.

There are often opacities in the cornea (Ware, v. Ammon).   Wharton Jones thought that acquired hydrophthalmia might be distinguished from congenital by the presence of opacities in the latter, and v. Muralt, Laclerc, and Picque considered that they were the cause of the disease. The opacities which are found are due to one of three causes, viz. increased intra-ocular tension, stretching, or intercurrent disease. Increased tension may lead to diffuse haze such as is met with in the glaucoma of the adult, and keratitis bullosa, etc., may supervene. Stretching of the cornea not infrequently leads to rupture of Descemet's membrane (*v.* Vol. I, p. 173, Fig. 108) and opacities which result from the repair of the injury.   Exposure of the cornea and malnutrition of the eye may lead to ulceration and scarring.

The condition of the sclerotic is a subject of dispute.   It has been stated that it may show no structural alteration, and that thinning is due only to distension, being most marked in the region of the limbus (Raab, Grahamer, Dürr and Schlegtendal).   True staphylomata are rare (Walter).   Heine and Marschke found an increase in thickness as compared with the emmetropic eye, an increase which could not merely be attributed to reaction to stretching, but was a veritable hyperplasia. Reis made careful measurements in seven cases.   Thinning of the corneo-scleral junction, as already mentioned, is conspicuous—*c. g.* 0·21 mm. to 0·38 mm.   Elsewhere there was distinct increase of thickness as compared with the normal, contrary to the experience of Gallenga, Baas, and Herrnheiser and Schnabel ; the latter authors generally

found thinning both in the anterior and posterior parts of the eye. It is not improbable that in the growing eye subjection to constant increased pressure may induce a compensatory hypertrophy, as, for example, in the heart.

The iris shows various stages of degeneration and atrophy, according to the duration of the disease; there is nothing characteristic of buphthalmia in the changes.

The ciliary body often shows traces of inflammation (Raab, Dürr and Schlegtendal, Gallenga, Kalt, etc.). It is usually more or less degenerated, and the ciliary muscle is atrophic. The ciliary processes may be intact or show evidence of degeneration. The changes are inconsistent with the hypersecretion theories.

The choroid is nearly always degenerated, often in marked degree. As usual, the smaller vessels suffer most, the larger vessels remaining long intact. In my experience choroidal hæmorrhage is a not infrequent reason for excision.

The retina is normal in the early stages, but such cases rarely come under anatomical observation. In most cases which have been examined there is atrophy, especially of the nerve-fibre layer. The rods and cones may be intact (Dürr and Schlegtendal), but have generally disappeared, only the nuclear layers remaining. Hæmorrhages are not uncommon in the retina. Detachment of the retina may occur (Dürr and Schlegtendal), probably usually owing to subretinal hæmorrhage.

The optic disc is invariably cupped, and is often extremely atrophic, though this is characteristic only of the later stages. The cupping differs in no essential from that found in glaucoma in the adult.

The condition of the angle of the anterior chamber is of prime importance. There can be no doubt that buphthalmia is the infantile form of glaucoma, and that the condition is due to increased intra-ocular pressure. The view that this is due to hypersecretion, held by Horner, v. Muralt, Gayet, Haab, Grahamer, Gallenga, Kalt, and Mayerhausen, is a priori improbable on the same grounds which hold good for adult glaucoma (q. v.). That, on the other hand, as in the adult form, the condition is due to defective filtration, there is now overwhelming evidence, and controversy rages rather about the exact cause and mechanism than about the fact.

The opinions of the earlier observers were much influenced by the current views about glaucoma in the adult. Thus, v. Muralt merely reproduces the nervous secretory theory of Donders, with the addition of a mechanical action upon the ciliary nerves brought about by the megalocornea. Dürr and Schlegtendal invoke the theory of interference with the venous outflow through the venæ vorticosæ, adding to the endo- and perivascular changes of Birnbacher and Czermak the effect of pressure by the oblique muscles. Schiess-Gemuseus held that any adhesion of a part of the uveal tract to the sclerotic might cause hydro-phthalmia. Grahamer invoked a primary uveo-cyclitis and Gallenga a primary choroiditis. Raab, whilst predicating a primary cyclitis, is conspicuous in laying stress upon the obliteration of the filtration angle, and Pflüger, whilst accepting an intra-uterine irido-choroiditis in his cases of aniridia, was not oblivious to the importance of blockage at

the iridic angle.   Manz attributed the disease to inflammation of the choroid and ciliary body, Kalt to chronic irido-choroiditis, leading to obliteration of vessels.   Other authors expressed similar opinions— Murray uveitis, May fœtal choroiditis, Venneman serous iritis, Gold- zieher choroiditis leading to sclerosis of the vessels.

Considering the deep anterior chamber and the apparently widely open angle in buphthalmia, it is not surprising that the peripheral anterior synechia which is often present should have escaped recogni- tion.   Pólya found that in 47 per cent. of the recorded cases the angle is said to have been open.   The most important evidence that the high tension in buphthalmia is due to defective filtration was adduced by Leber and Bentzen, when they showed by actual experiment that the

FIG. 770.—BUPHTHALMIA.
From a photograph by Coats.   Angle of the anterior chamber.

rate of filtration in a buphthalmic eye was considerably below the normal.   Anatomical investigations show that, though the angle may be apparently open, it differs profoundly from the normal condition (Treacher Collins, Cross, Römer, Gross, Reis).   Horner (1889) first put forward the view that buphthalmia might be due to some congenital abnormality of the angle of the anterior chamber.   Gros accepts the opinion of Treacher Collins that there is imperfect separation of the iris from the cornea at the periphery, due to arrested development. Römer, Gross, and especially Reis, lay more stress upon aplasia of the canal of Schlemm, which is frequently absent, partially or completely. It cannot be said to be disproved that in some cases peripheral anterior synechia and obliteration of the canal of Schlemm may be due to intra-

uterine inflammation, but it is extremely difficult to decide whether inflammatory changes are primary or secondary.

It has already been mentioned that the angle of the anterior chamber resembles that of lower mammals during early fœtal life (Vol. I, p. 282). The ligamentum pectinatum iridis then consists of two parts—an outer, more compact, part lying in apposition with the sclerotic and forming the inner wall of the canal of Schlemm, and an inner, looser, part. The latter persists in man until the sixth month (Rochon-Duvigneaud, Treacher Collins), after which it disappears, and with it disappear most of the spaces of Fontana. Rochon-Duvigneaud called the outer persistent portion the sclero-corneal trabecular system, and looked

FIG. 771.—BUPHTHALMIA.
From a photograph by Lister. Angle of the anterior chamber, showing adhesion of the root of the iris.

upon it as derived by dissociation from the inner circular lamellæ of the sclerotic.

From a careful examination of the angle in a large variety of mammals Treacher Collins found that the ligamentum pectinatum is much more extensive than in man. It consists of an external laminated zone with slit-like spaces and an inner cavernous zone with large irregular spaces. In man the cavernous zone is practically absent, the angle of the anterior chamber being prolonged farther outwards than in mammal's eyes. This alteration is associated with an alteration in the relative size of the cornea and globe. The decrease in the relative size of the cornea to the globe in man is thus accompanied by a simplification of the ligamentum pectinatum and a prolongation of the anterior chamber outwards. In the process of development of the human eye it passes through stages in which the relation of parts about

the angle of the anterior chamber and the relative size of the cornea to the globe are the same as in lower mammals—a further example of the dictum that ontogeny is a compressed phylogeny.

In some congenitally defective human eyes in which the globe has failed to reach its normal dimensions, the condition of parts about the angle and the relation of the size of the cornea to that of the globe which exist before birth and which are found in the eyes of the lower mammals persists (Fig. 772).

Treacher Collins in his examination of buphthalmic eyes came to the conclusion that there was an incomplete separation of the iris from the cornea. He is now rather inclined to think that the condition is

FIG. 772.—FŒTAL CONDITION OF THE ANGLE.   × 18.

Parsons, T. O. S., xxii. From a case of microphthalmia. The angle is filled with spongy tissue, containing well-marked spaces of Fontana; this extends well in front of Schlemm's canal. Other features showing arrest of development are seen in the persistence of the posterior vascular sheath of the lens and the condition of the pars ciliaris retinæ.

better ascribed to an abnormal persistence of the prehuman or prenatal condition of the ligamentum pectinatum. This is supported by the fact that in many cases (Treacher Collins, Cross, and others) strands of tissue stretch between the base of the iris and the cornea (Figs. 771. 773). Collins attributes this to persistence of part of the cavernous area. He considers that the prolongation outwards of the anterior chamber in the normal human eye facilitates the exit of aqueous, and that this is rendered necessary by the diminished area which the ligamentum pectinatum occupies in proportion to the size of the eyeball. If the prenatal condition persists in an eye which is congenitally small. no delay in the exit of fluid from the eye results and the tension remains normal; if, on the other hand, the eyeball attains an average size, then

delayed exit of fluid occurs, and increase of tension with enlargement of the globe results.

Obliteration of the venous network of Schlemm has been described by several authors, but particular stress has been put upon the phenomenon by Reis. Römer found the canal of Schlemm absent over one fifth of the whole circumference in one case, and Gross found it completely absent. Reis found more or less obliteration in seven cases. He considers that buphthalmia is essentially due to aplasia of this venous network. It is very doubtful if this is not a sequel rather than a cause. It is not infrequent to find undoubted evidence of inflammatory changes in and about the angle as well as in other parts of the eye. The partial or even complete obliteration of the canal of Schlemm
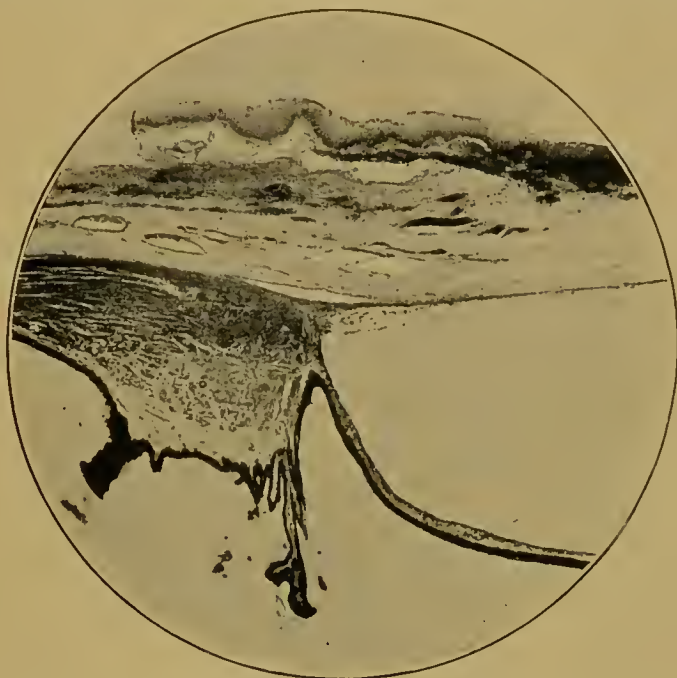
FIG. 773.—BUPHTHALMIA.
From a photograph by Lister. Angle of anterior chamber.

in old cases of glaucoma in the adult is well known and is almost certainly secondary. Just as it is impossible in many cases to decide whether the inflammatory changes which are met with are primary or secondary, so also in the case of the obliteration of the canal of Schlemm.

Whatever be the exact mechanism, it would seem to be certain that there is a very definite obstruction to the filtration of lymph from the eye at the angle of the anterior chamber in buphthalmia. Whether this is due to a congenital arrest of development or to intra- or early extra-uterine inflammation must, I think, be left an open question. It may be remarked that even an arrest of development must have some cause, and that this is most probably to be discovered in some intra-uterine inflammatory or toxic condition.

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